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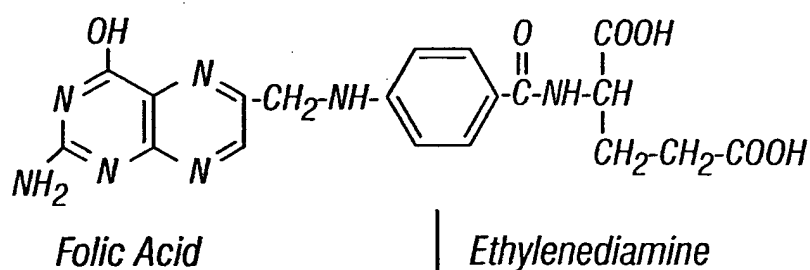
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Ethylenediamine
 EEDQ

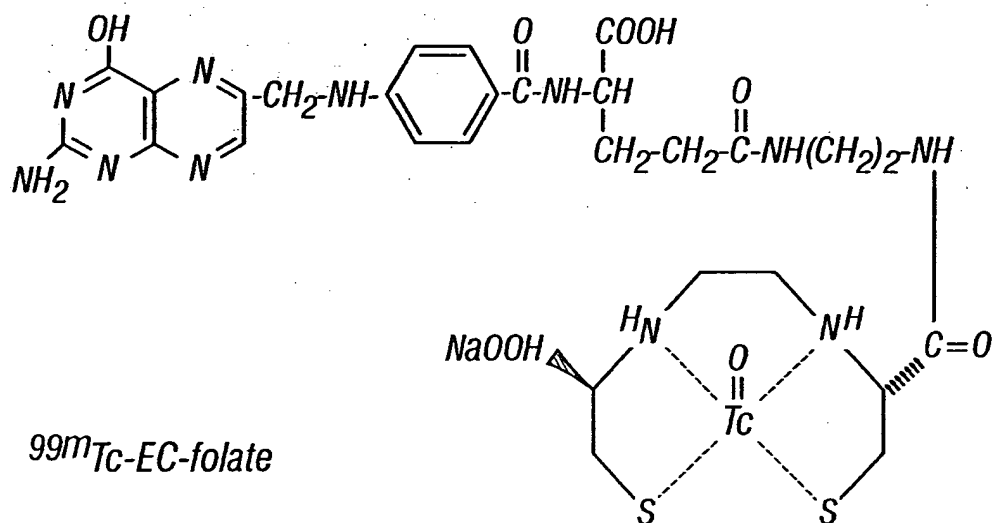
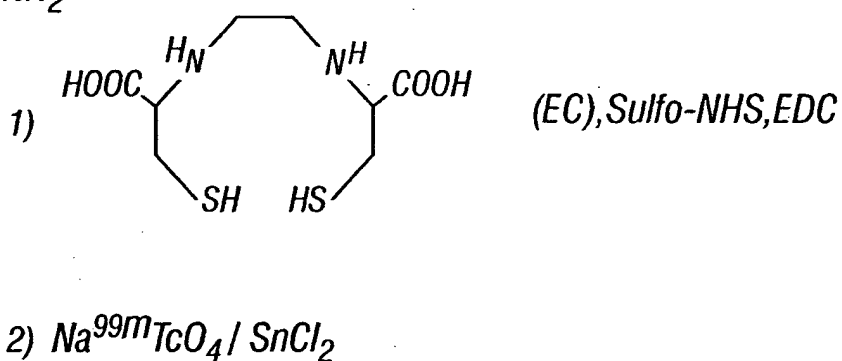
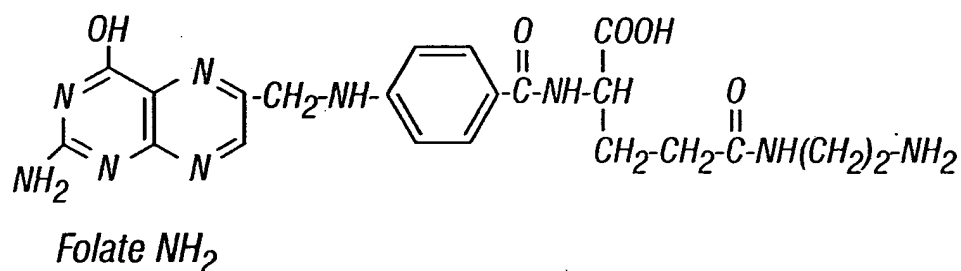


FIG. 1

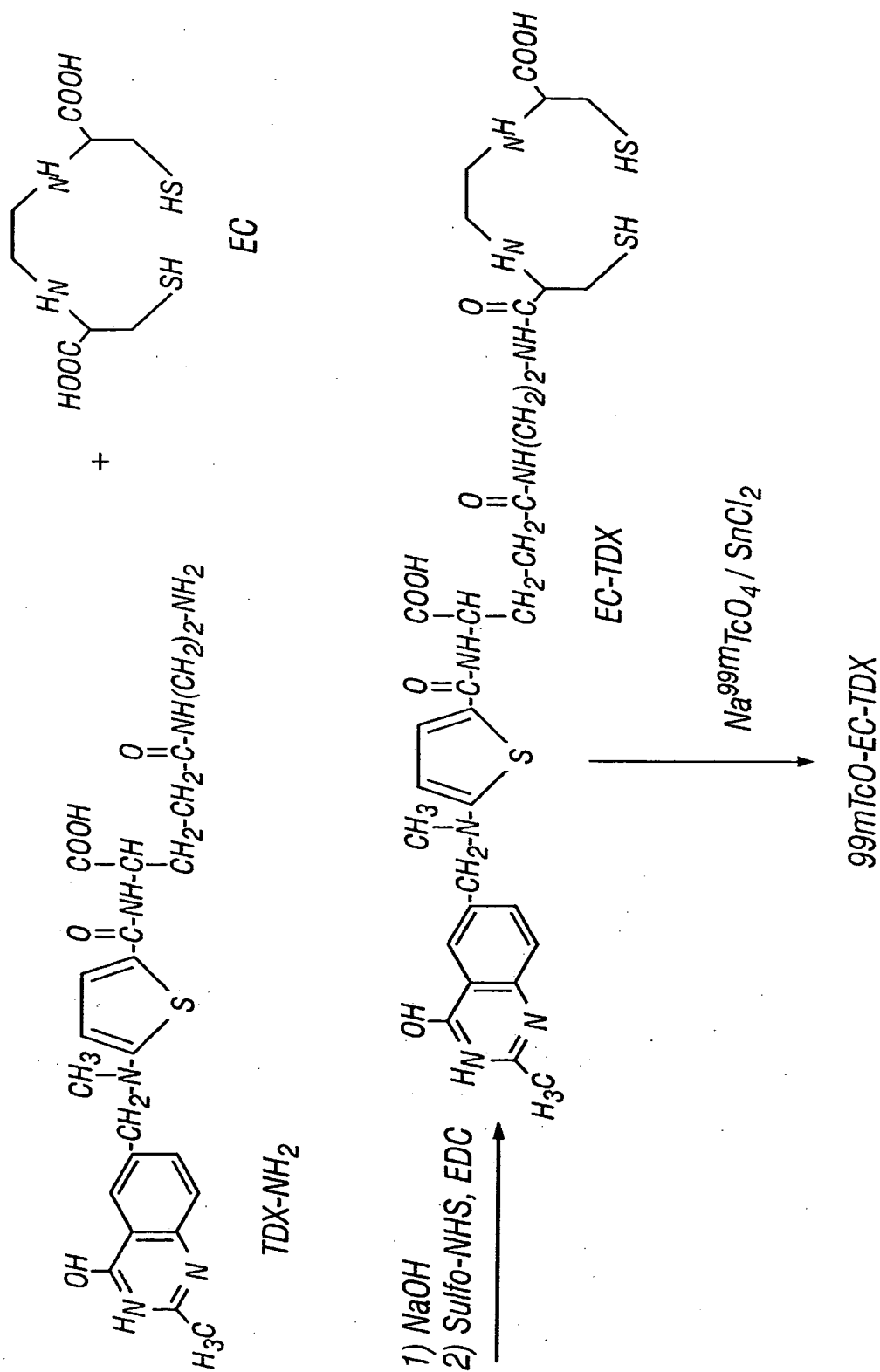


FIG. 3

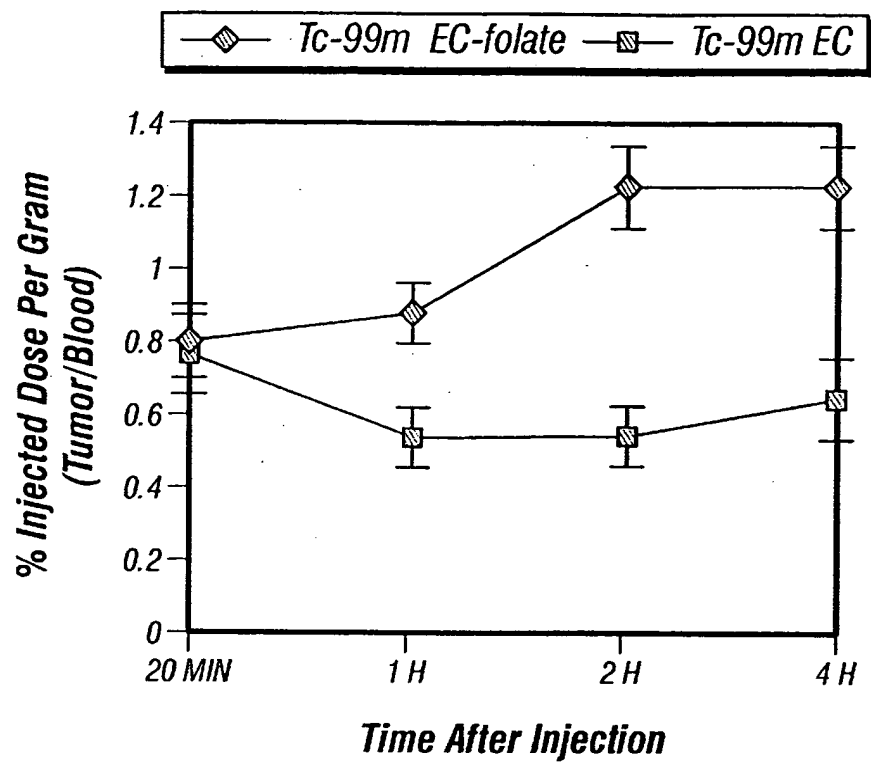


FIG. 4

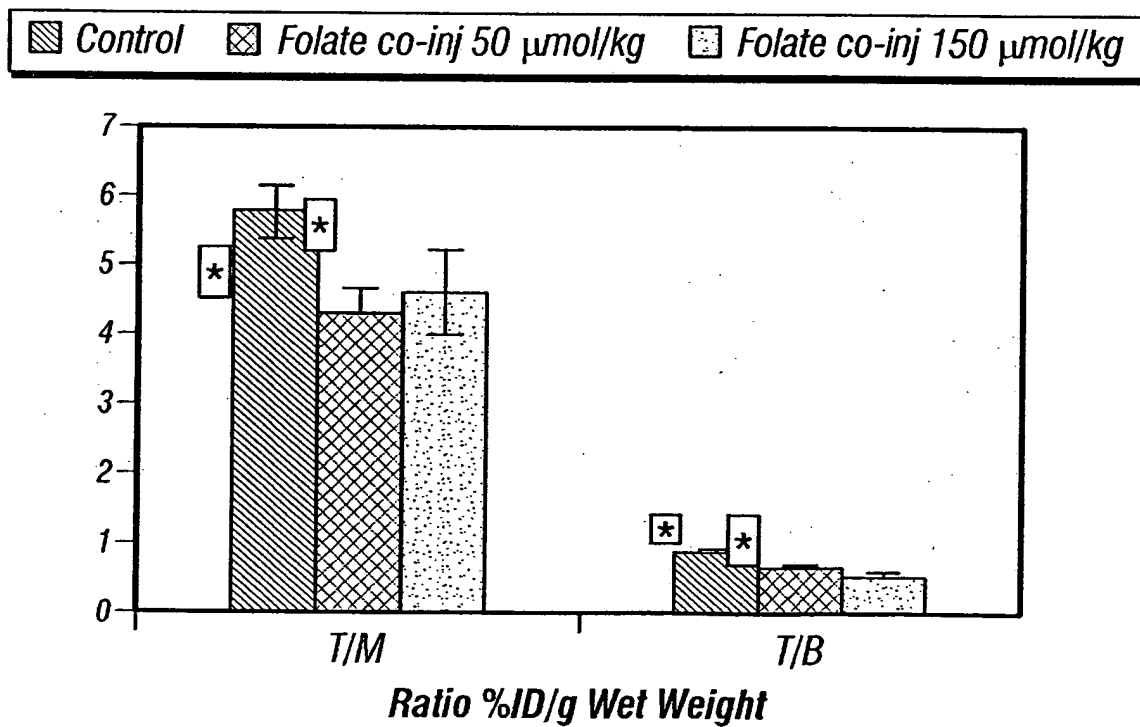


FIG. 5

Tc-99m EC

Tc-99m EC-folate

Tc-99m EC

Tc-99m EC-folate

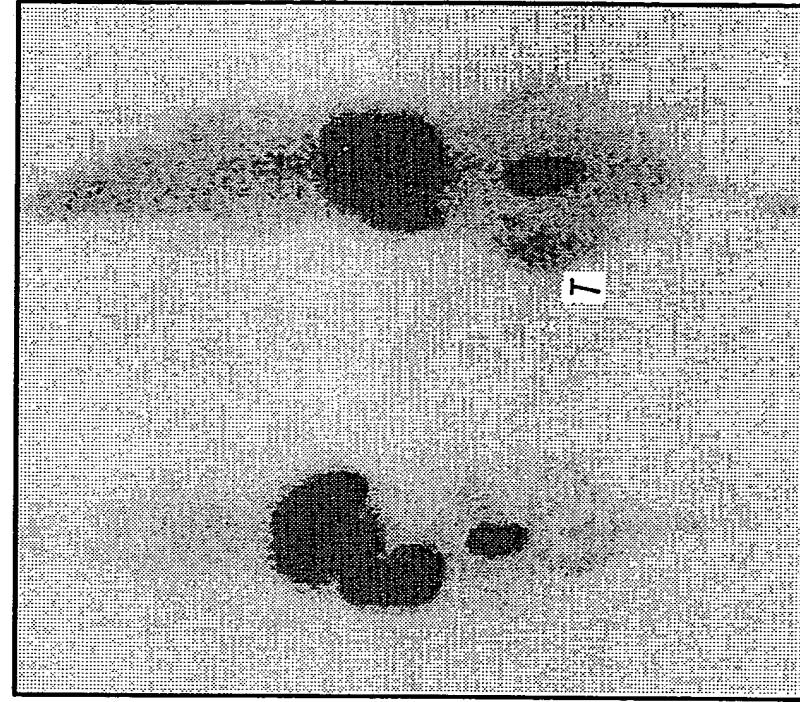
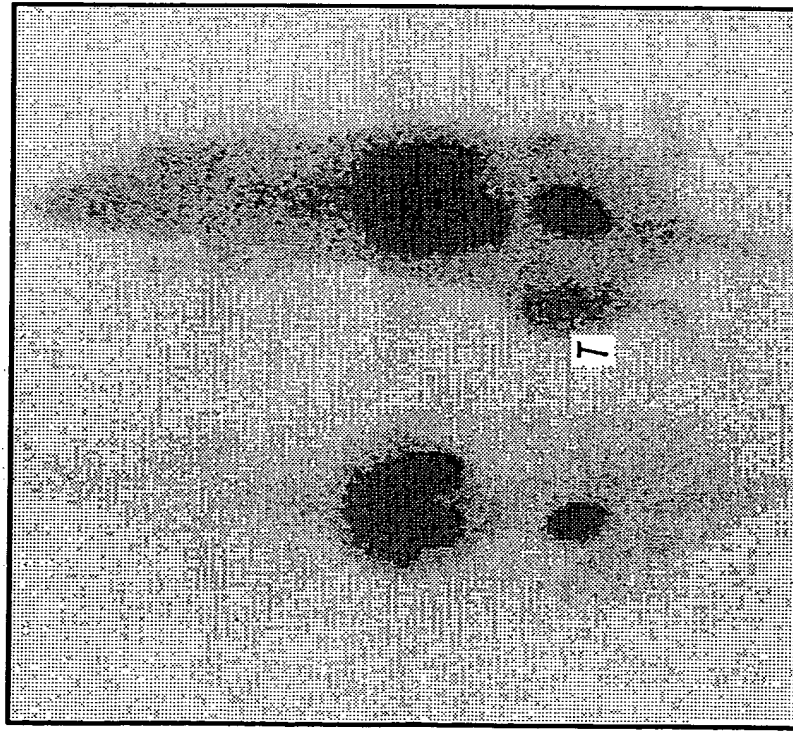


FIG. 6A

FIG. 6B

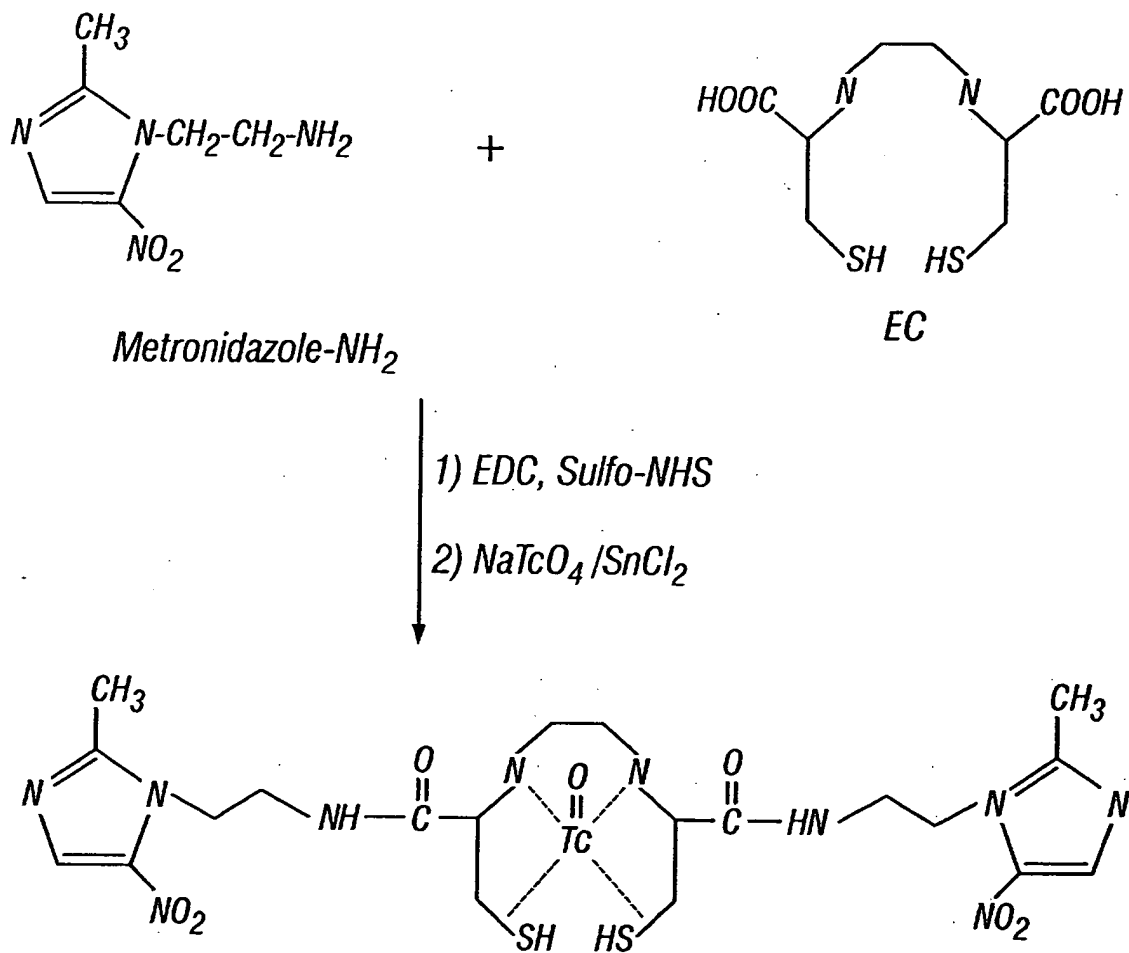
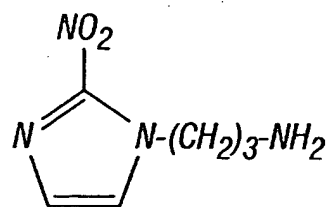
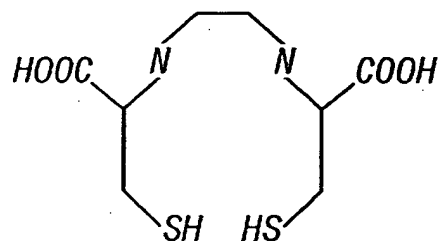


FIG. 7



2-Nitroimidazole-NH₂



EC

1) EDC, Sulfo-NHS
2) NaTcO₄ / SnCl₂

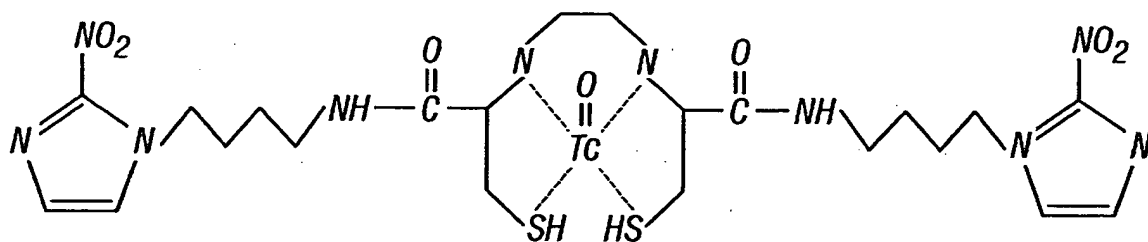


FIG. 8A

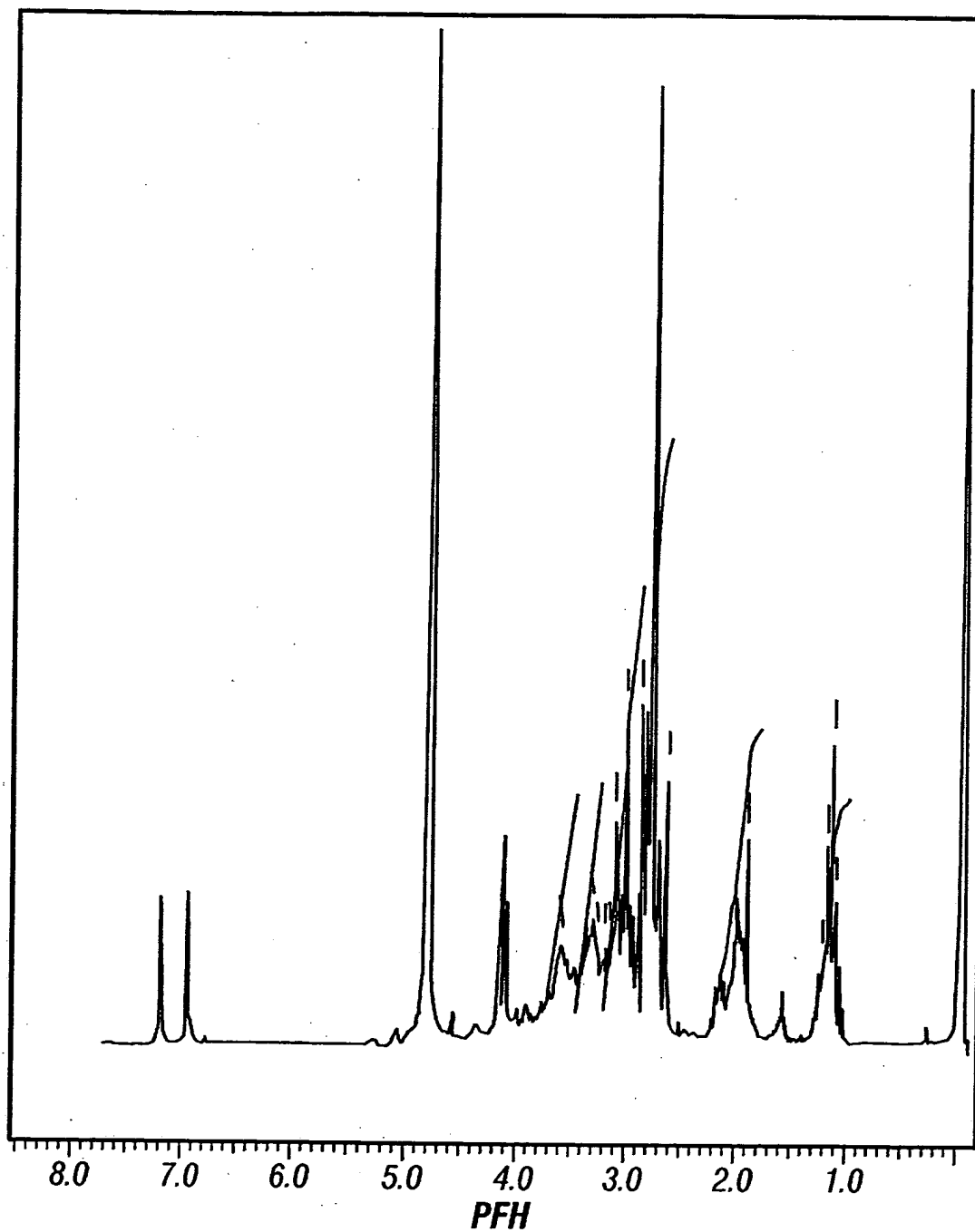


FIG. 8B

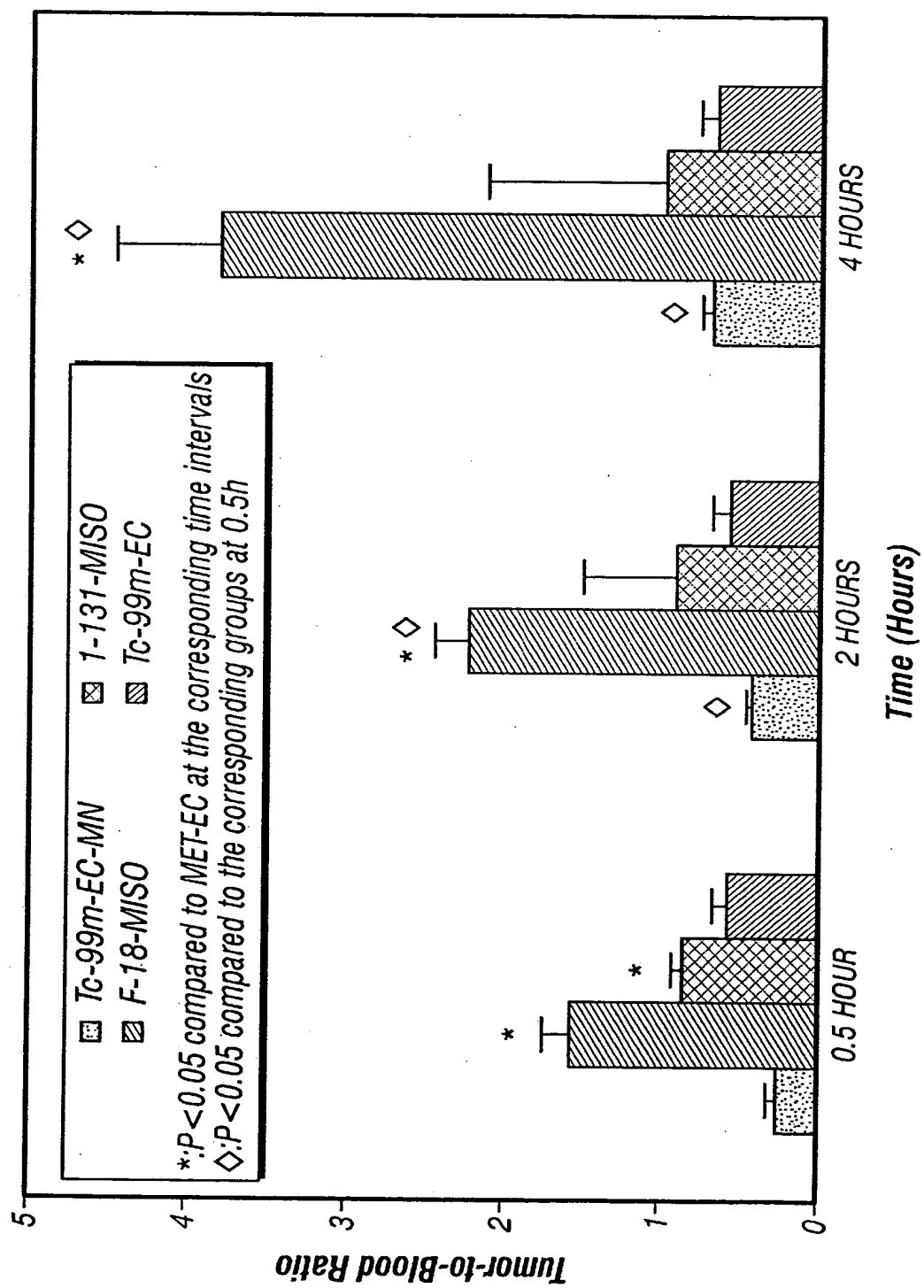


FIG. 9

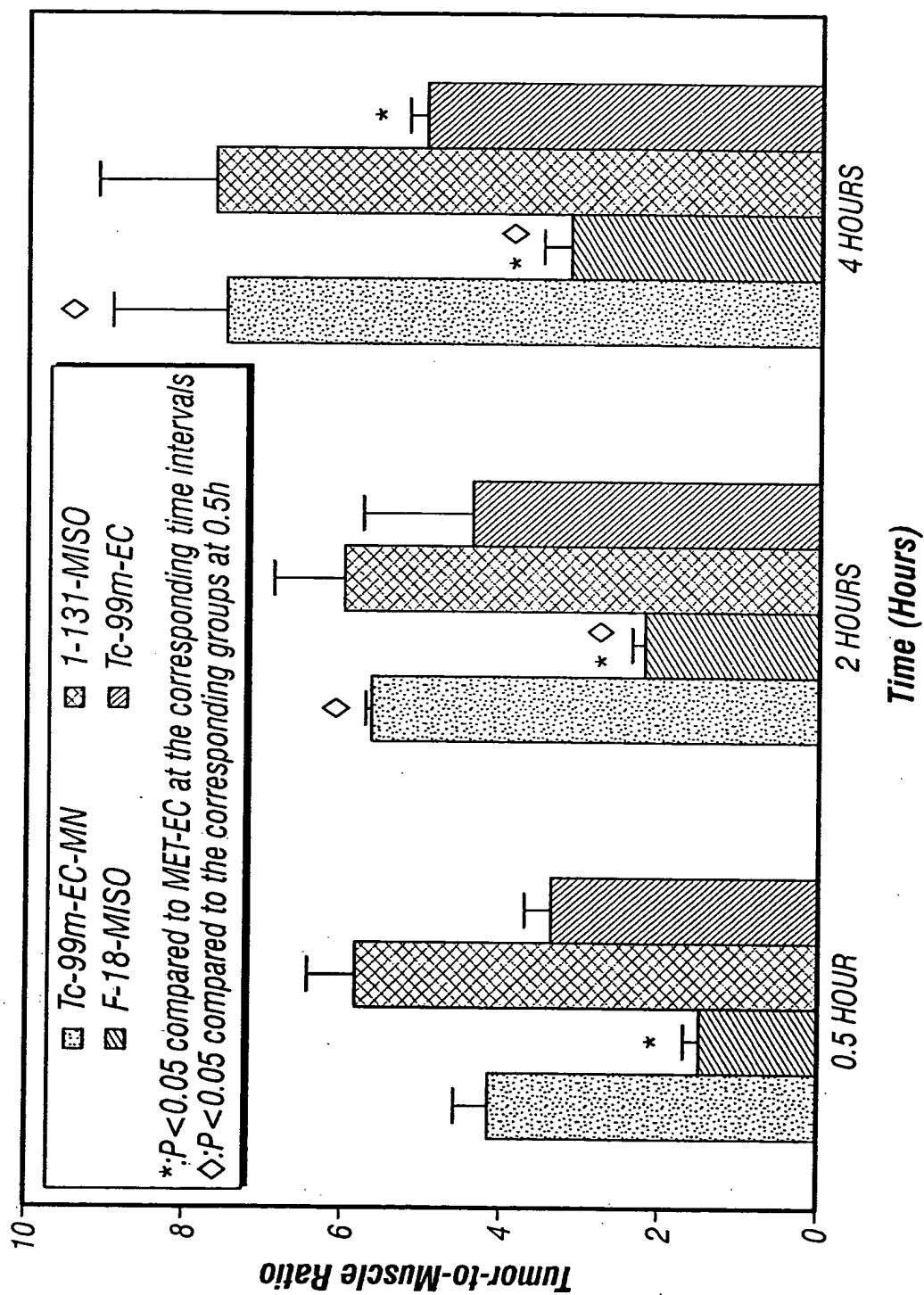


FIG. 10

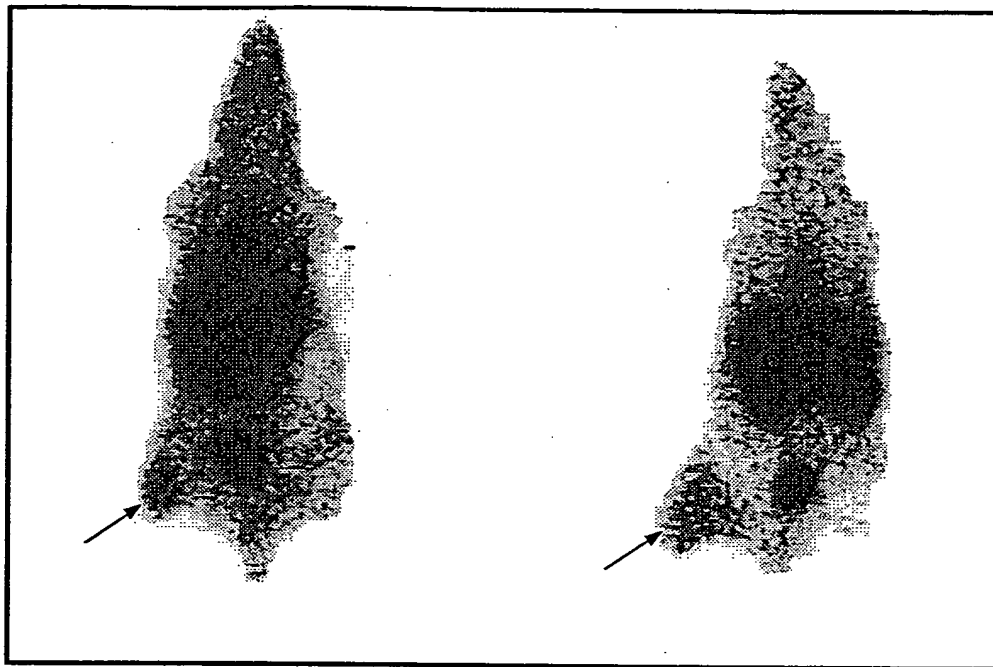


FIG. 11A

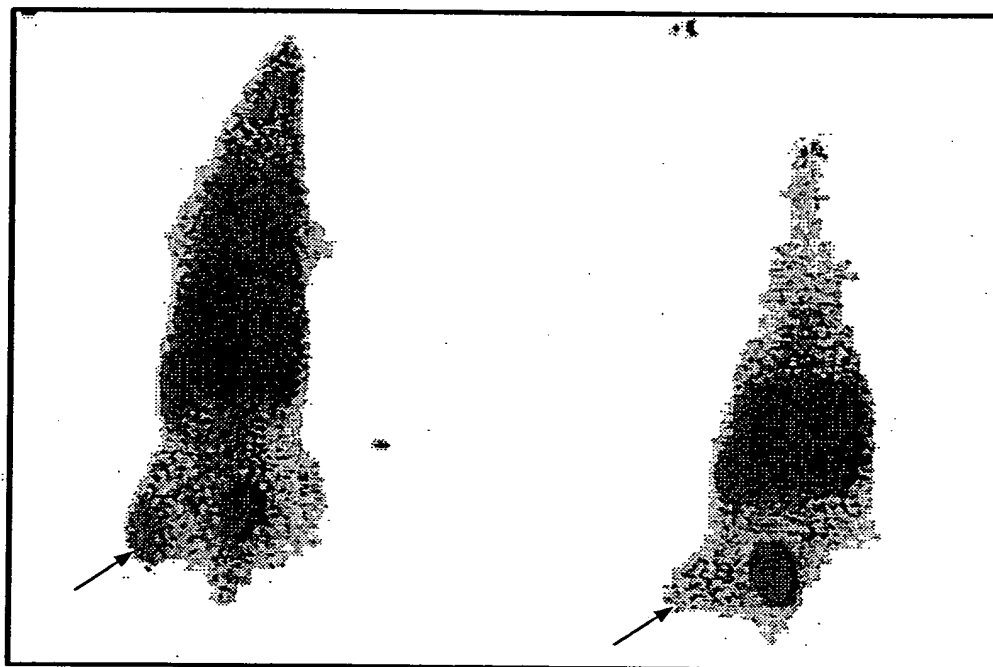


FIG. 11B

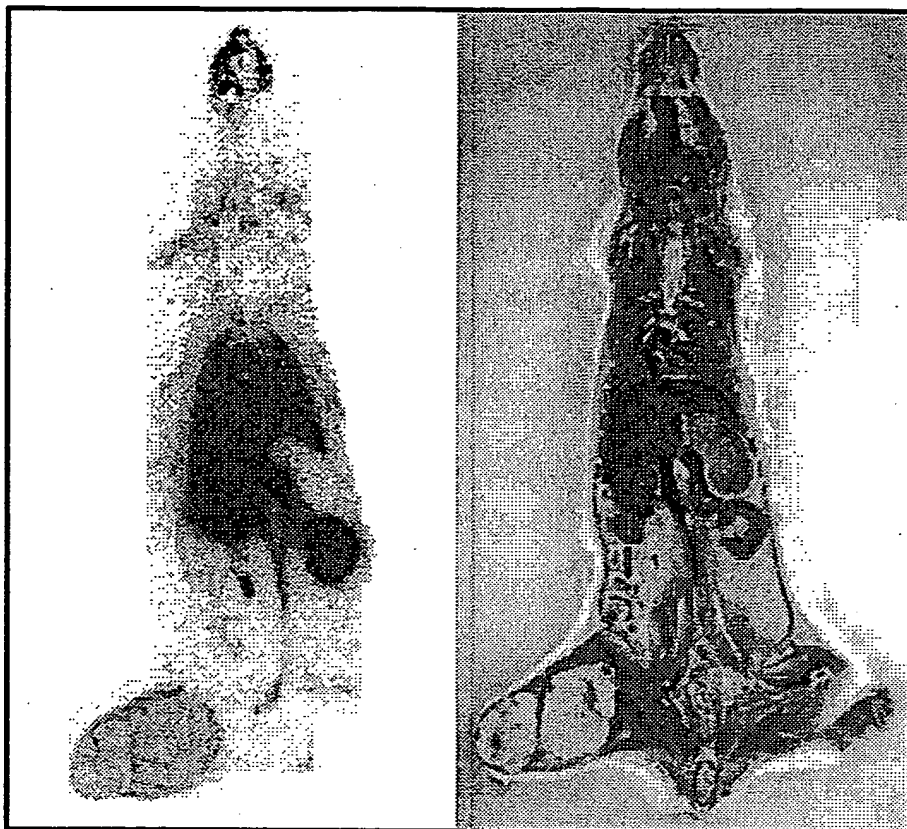


FIG. 12

3-10-1999

EC-(2-¹⁴C) after adding serum 3.

Date: Mar 10 1999

Start time: 16:02

Accum time: 00:00:50

Data File:

Plate: 1 Lane: 1

Elect Resolution: NORMAL

(Amp. Range: 0 - 2047)

Stop counts: 50000

Stop Counts Region: 0.00 to 20.00 cm

Rf Calculations: Origin: 1.50 cm

Solvent Front: 19.00 cm

Integration Parameters: Auto Integration

Peak slope: 1.0

Min width: 0.1

Min %: 2.0

Total Count Region: 0.00cm to 20.00cm

Total Counts: 53170

Total CPM: 63810

Reg. #	Start (cm)	Stop (cm)	Center (cm)	Rf	Region Counts	Region CPM	% of Tot Reg	% of Tot Cn
1	0.60	4.40	2.50	0.06	4557	5468	9.02	8.5
2	8.20	16.80	12.56	0.63	45980	55180	90.98	86.4
TOTAL					50540	60650	100.00	95.0

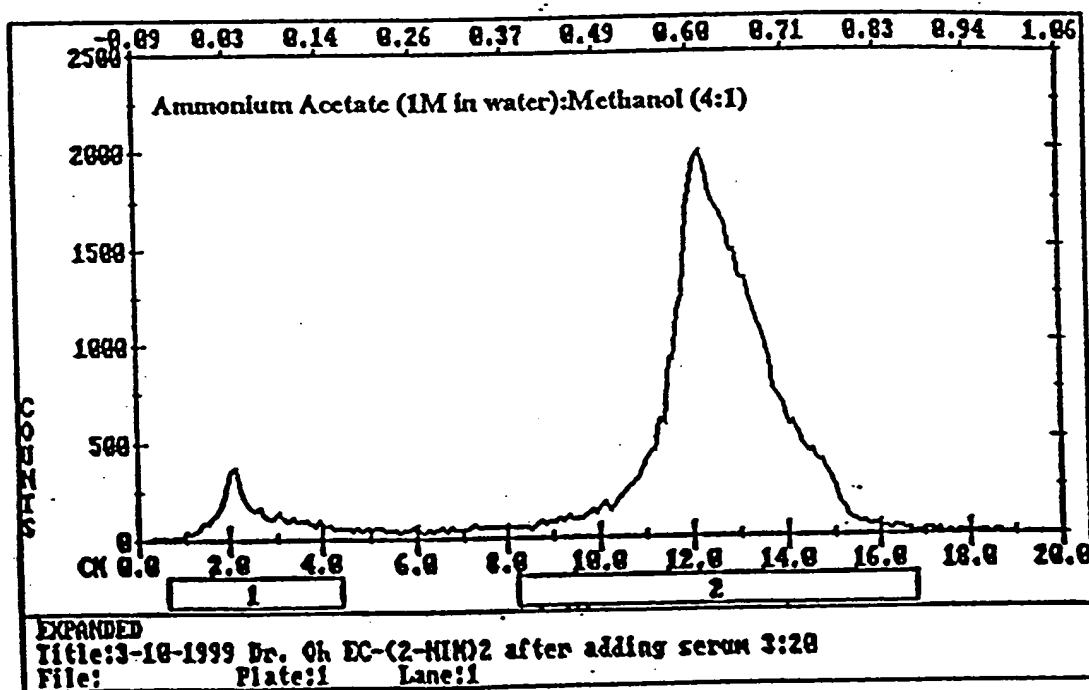
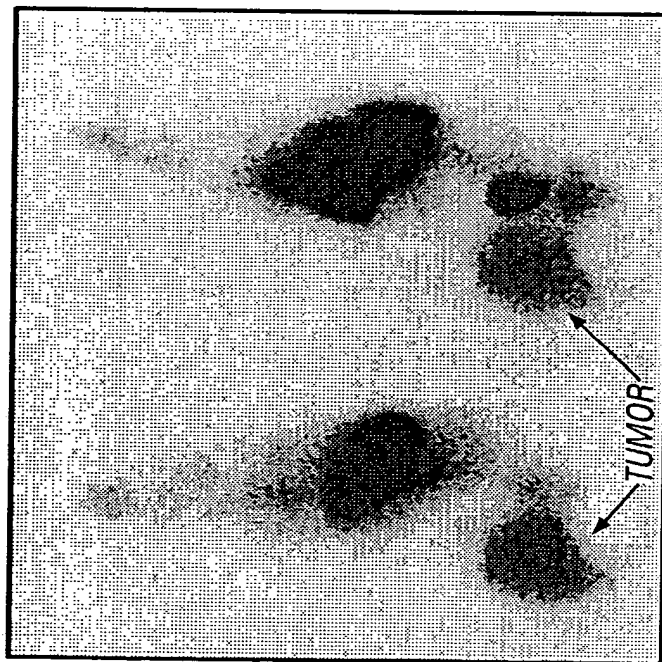
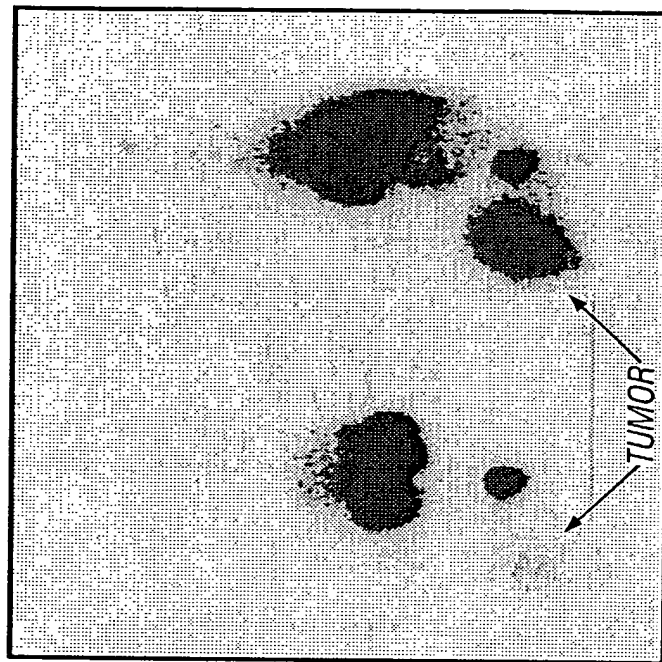


FIG. 13

$^{99m}\text{Tc-EC}$ $^{99m}\text{Tc-EC-NIM}$ $^{99m}\text{Tc-EC}$ $^{99m}\text{Tc-EC-NIM}$



15 MIN.



4 HOUR

FIG. 14A

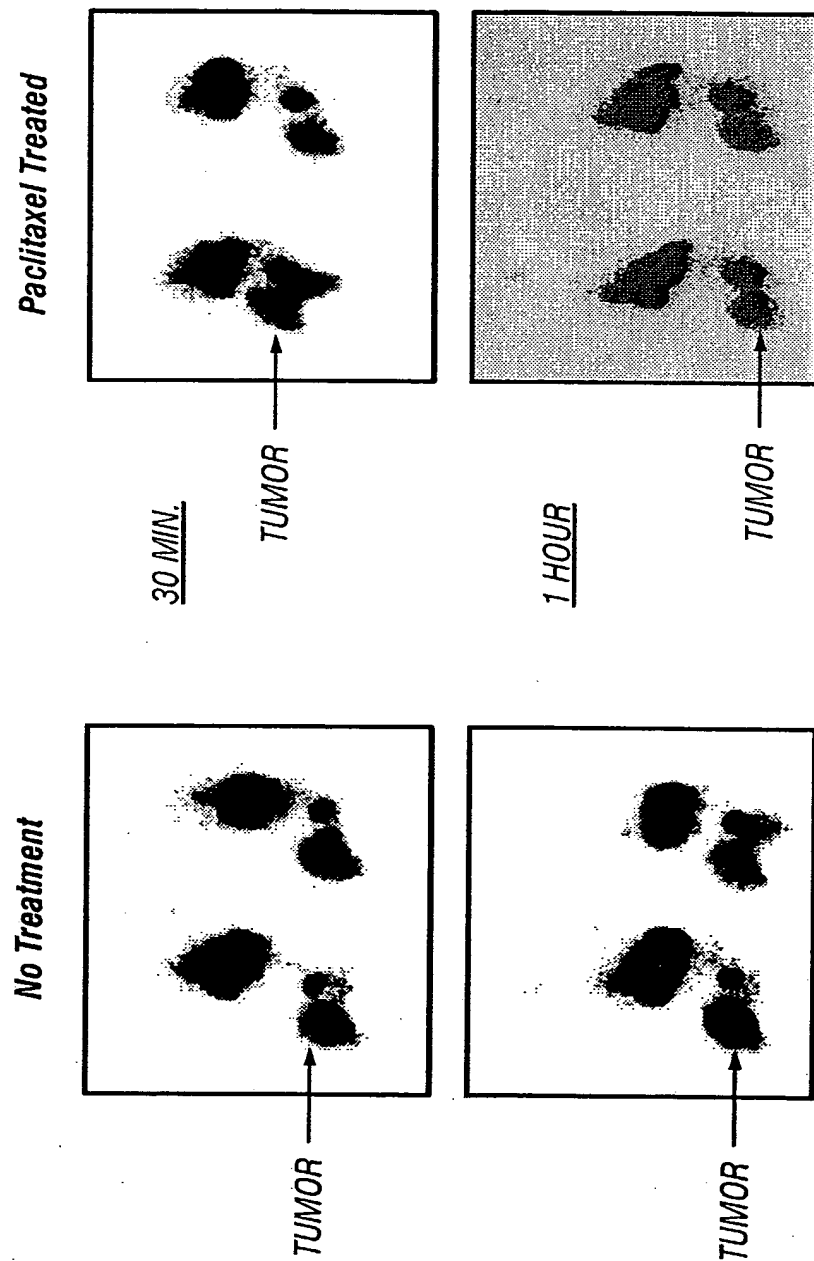


FIG. 14B

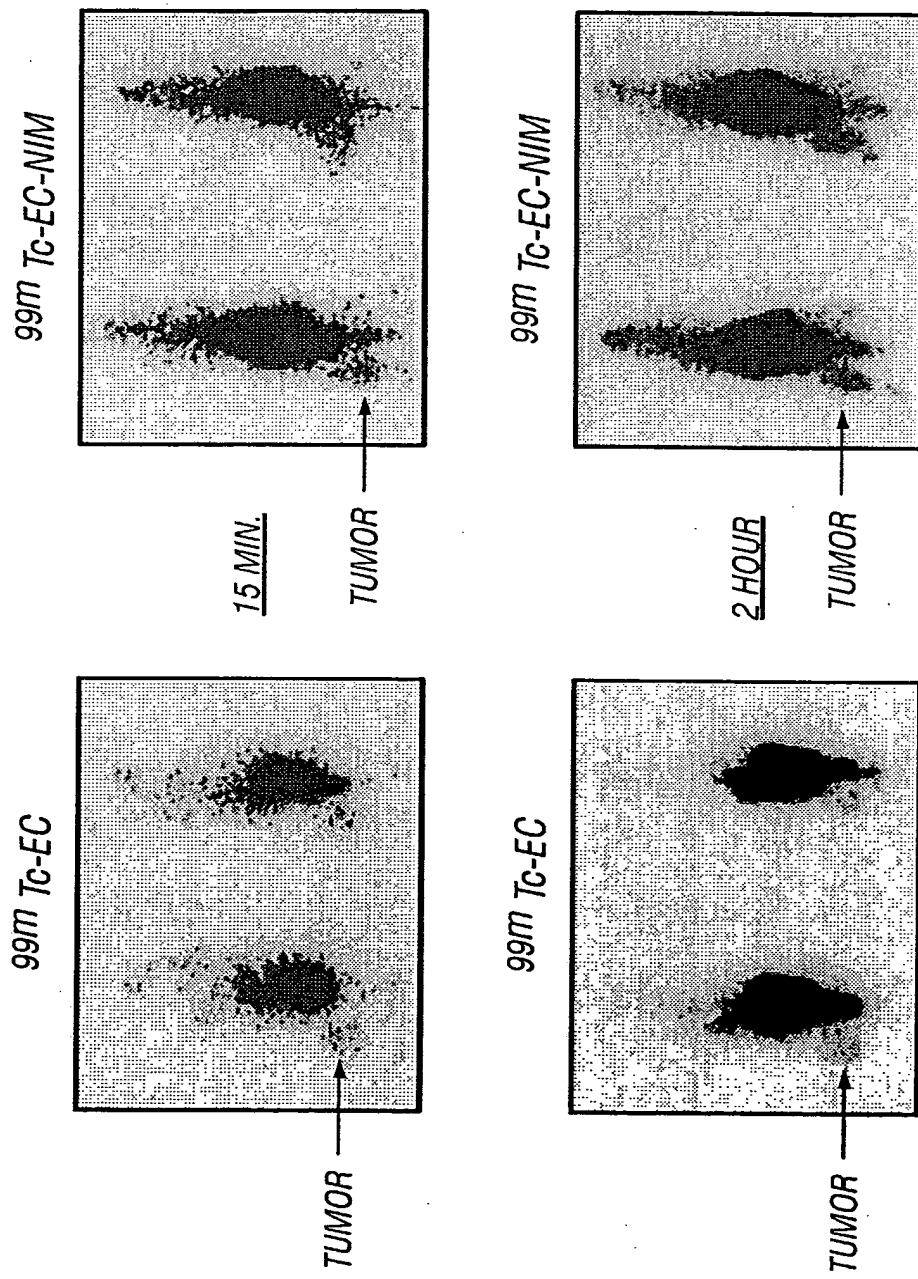


FIG. 15A

99m Tc-EC-Nitroimidazole (NIM)
(100 μ Ci/mouse, iv.)

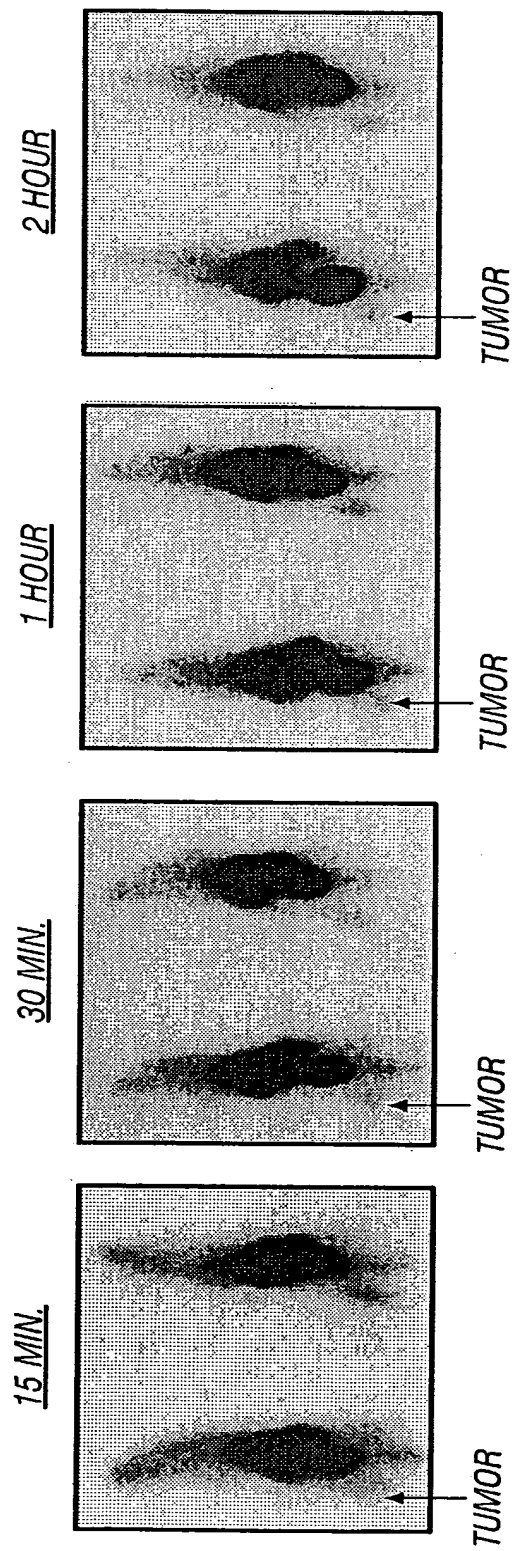


FIG. 15B

^{99m}Tc-EC-Nitroimidazole (NIM)

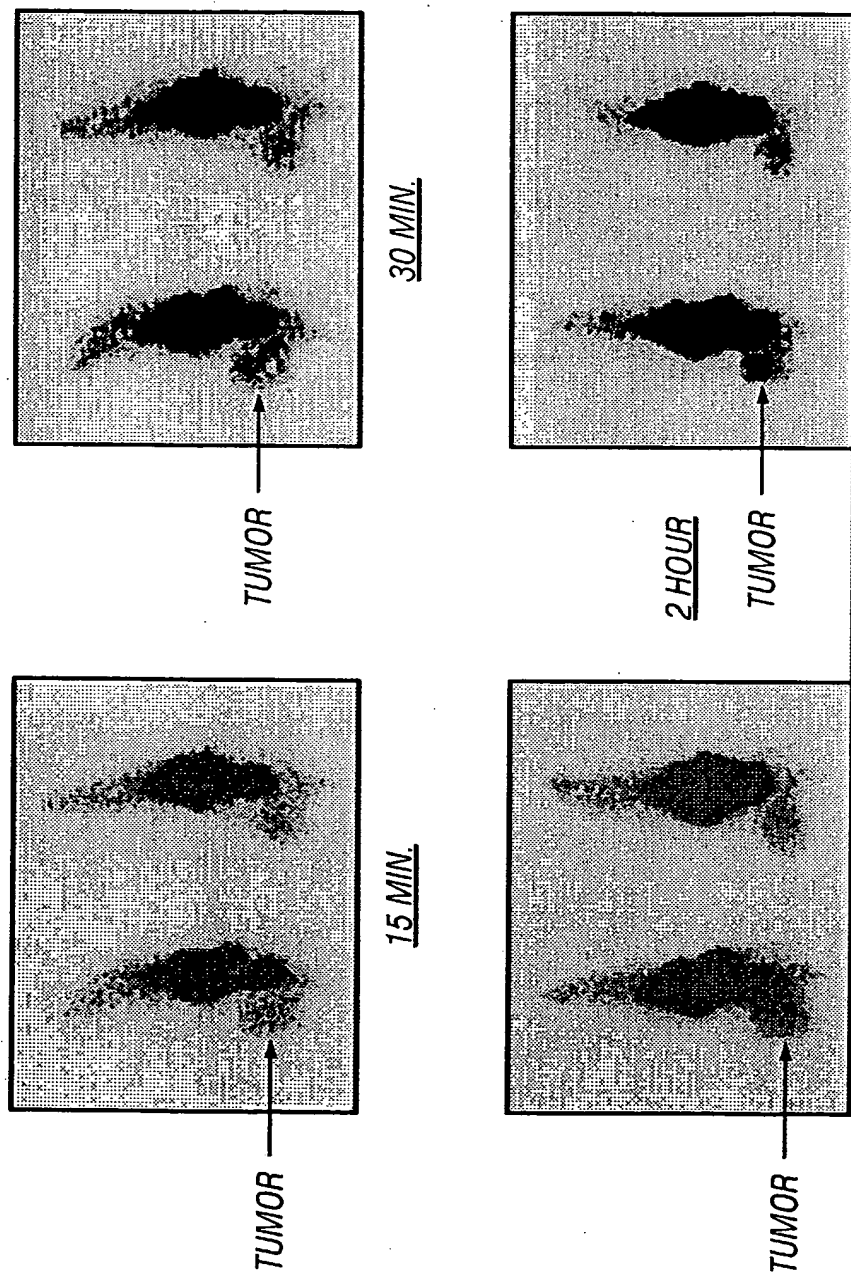
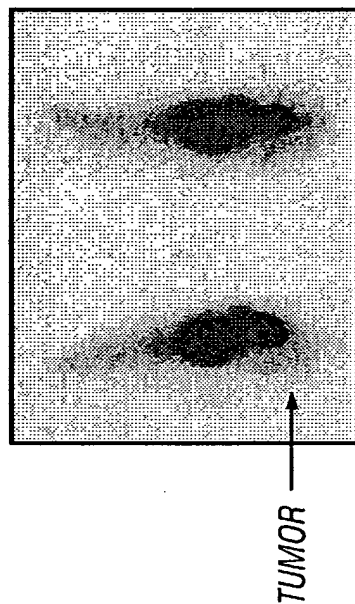


FIG. 15C

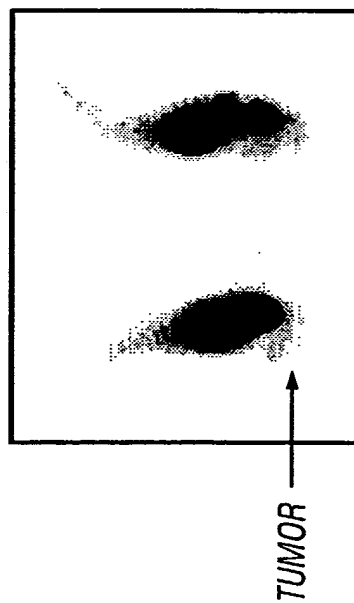
*^{99m}Tc-EC-Nitroimidazole (NIM)
(100 μ Ci/mouse, iv.)*



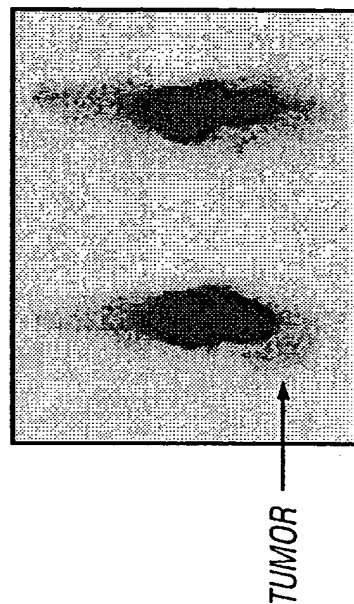
15 MIN.



30 MIN.

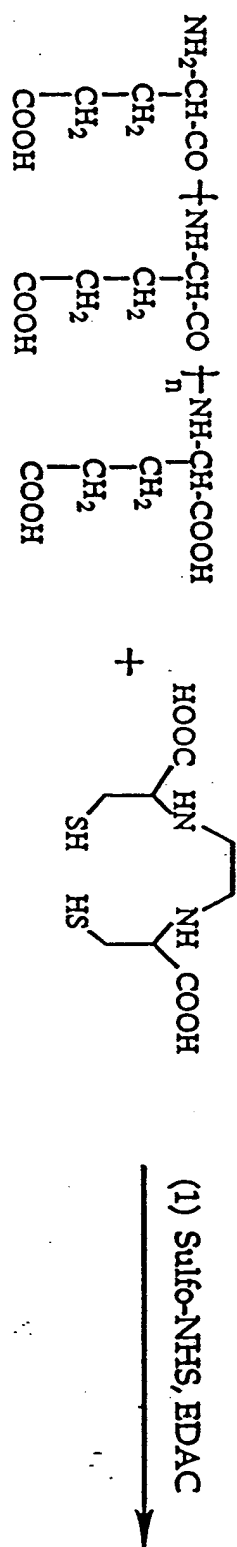


1 HOUR



2 HOUR

FIG. 15D



L-GAP

EC

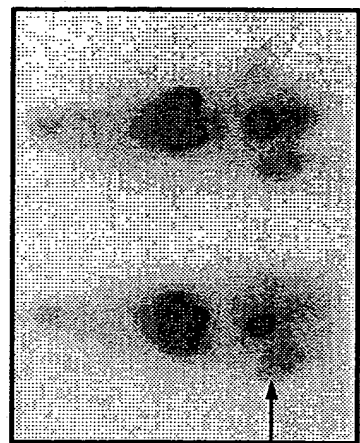


EC-GAP

Synthesis of EC-GAP

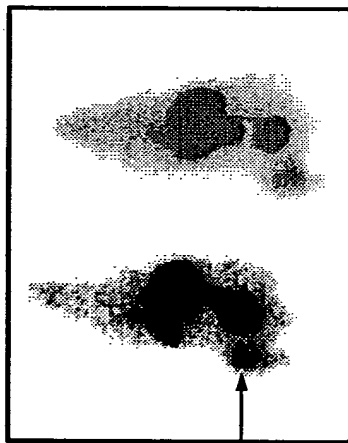
FIG.

16



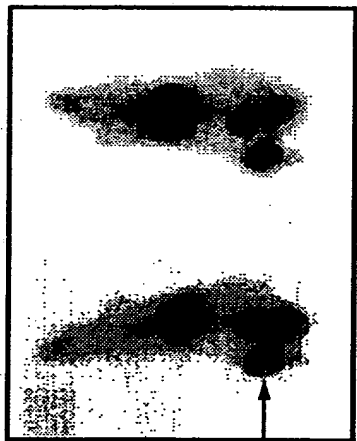
30 MIN.

TUMOR



2 HOUR

TUMOR



15 MIN.

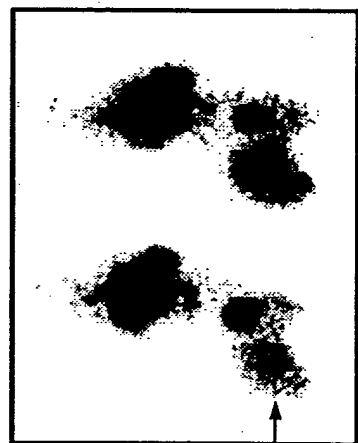
TUMOR



1 HOUR

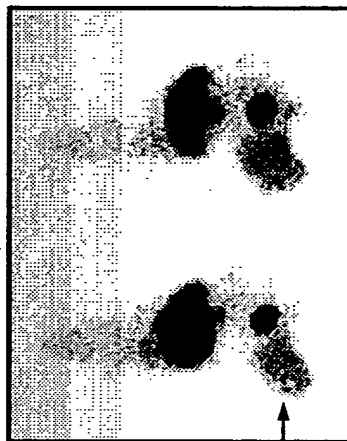
TUMOR

FIG. 17



30 MIN.

TUMOR



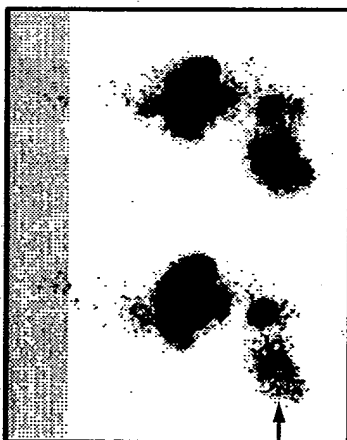
2 HOUR

TUMOR



15 MIN.

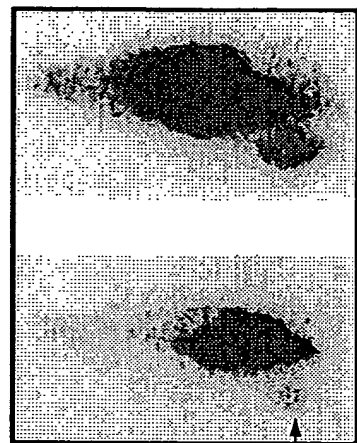
TUMOR



1 HOUR

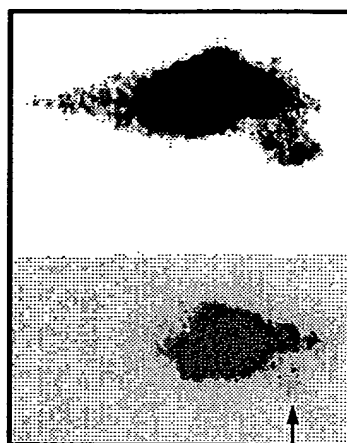
TUMOR

FIG. 18



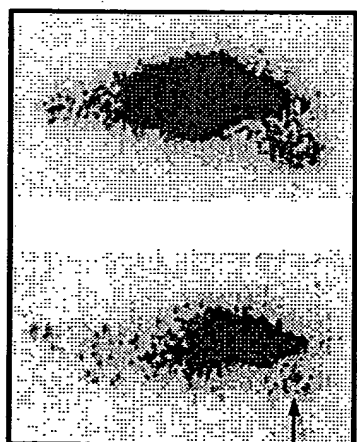
TUMOR

30 MIN.



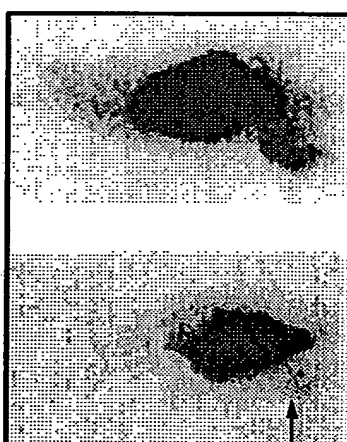
TUMOR

2 HOUR



TUMOR

15 MIN.



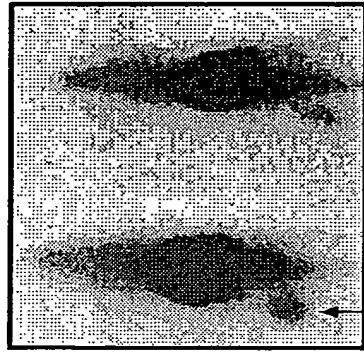
TUMOR

1 HOUR

FIG. 19A

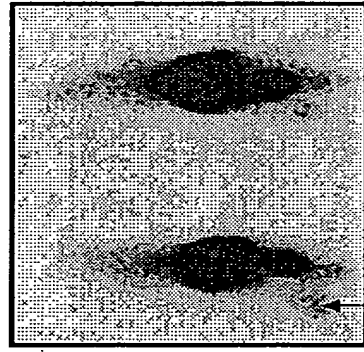
^{99m}Tc -EC-Annexin V
($100\mu\text{Ci}/\text{mouse}$, iv.)

15 MIN.



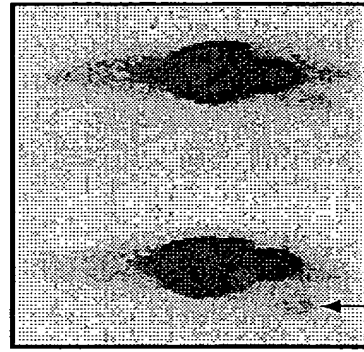
TUMOR

30 MIN.



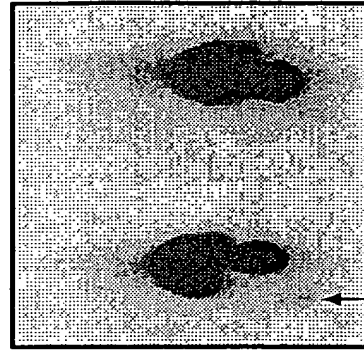
TUMOR

1 HOUR



TUMOR

2 HOUR



TUMOR

FIG. 19B

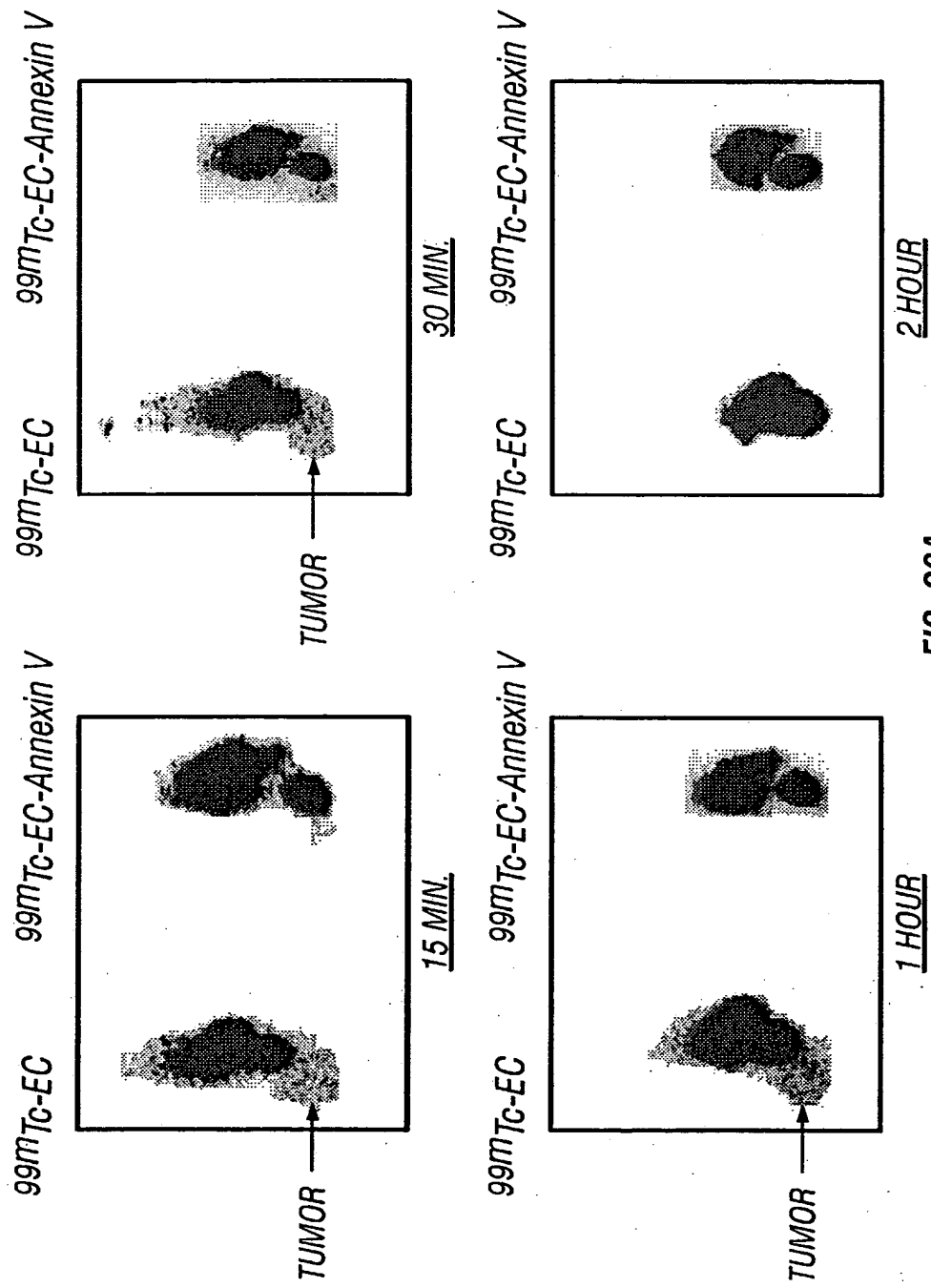


FIG. 20A

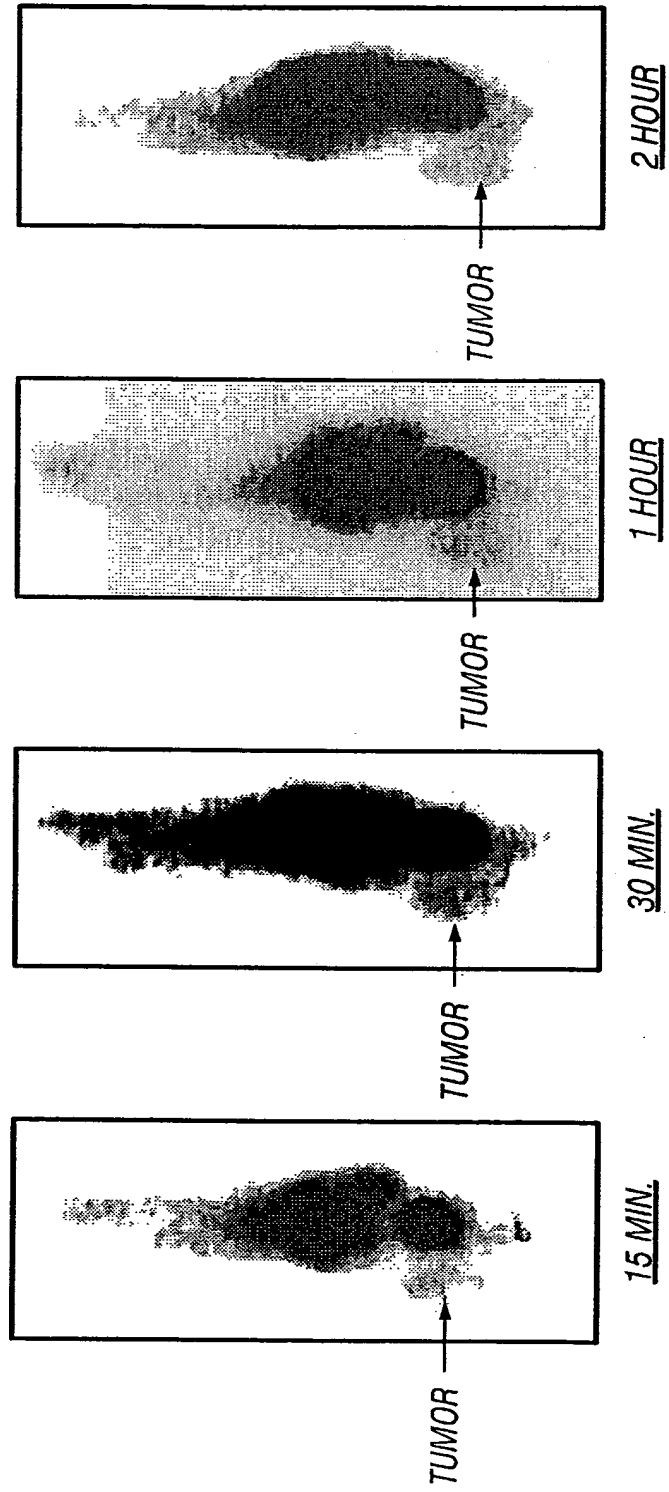


FIG. 20B

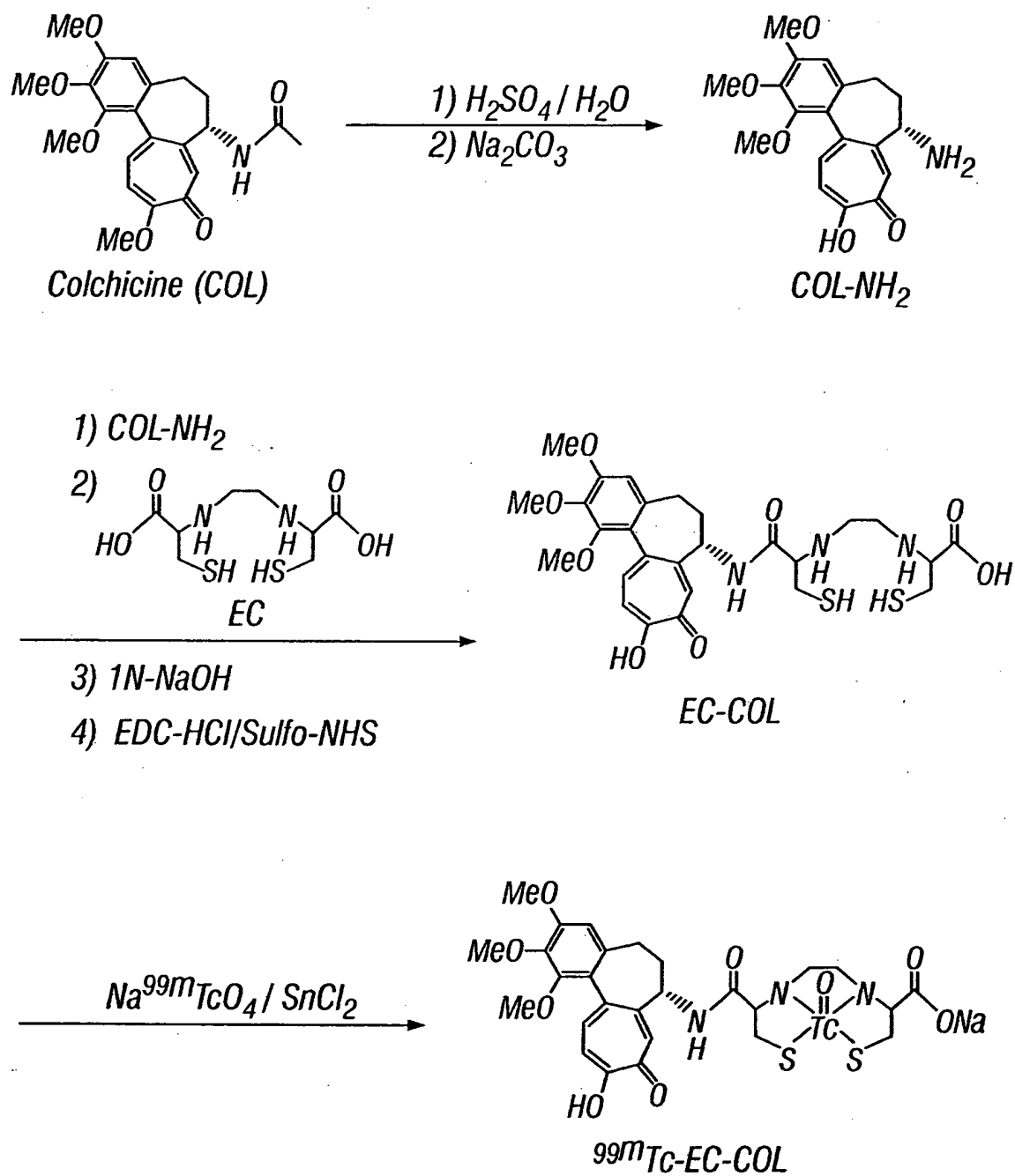


FIG. 21

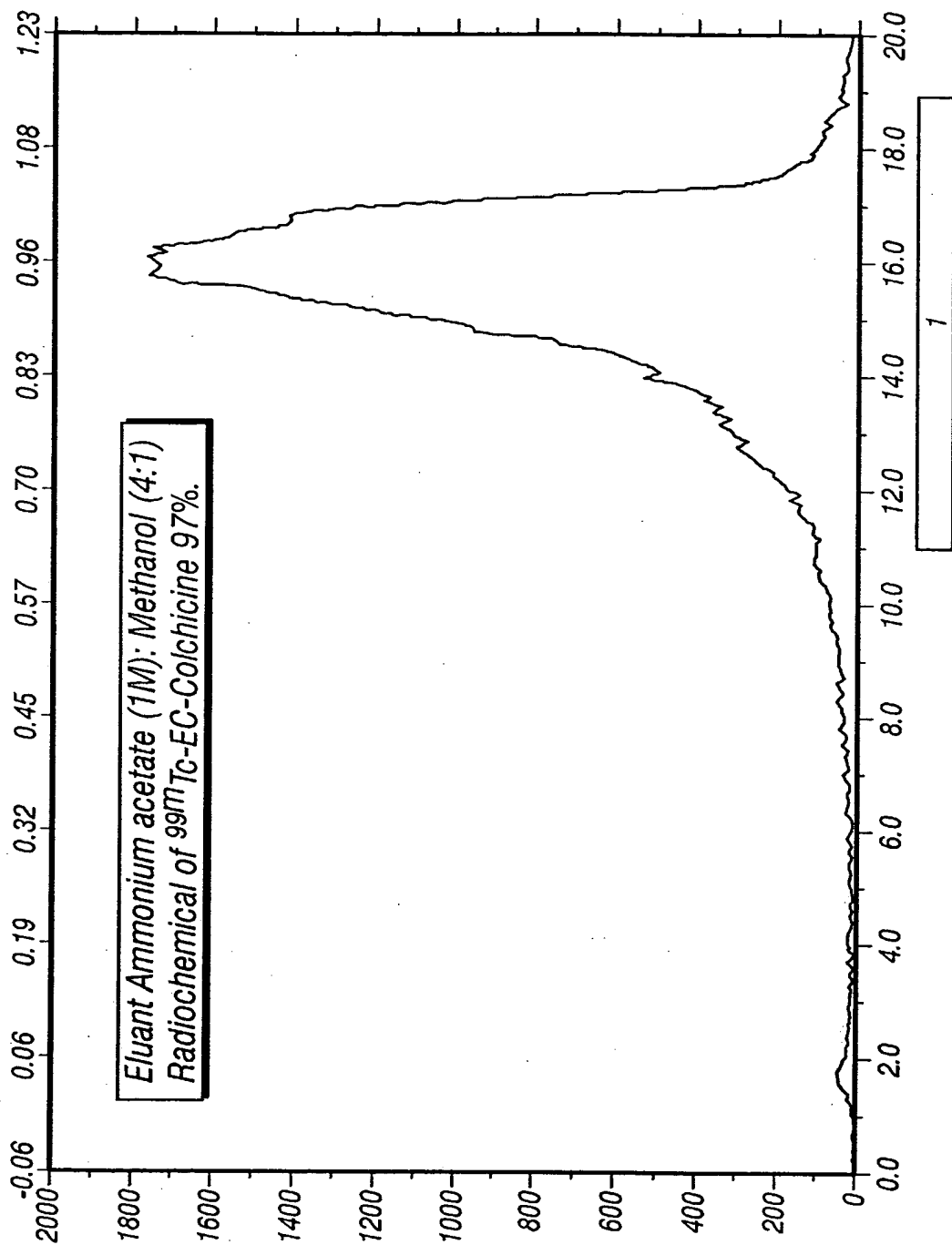


FIG. 22

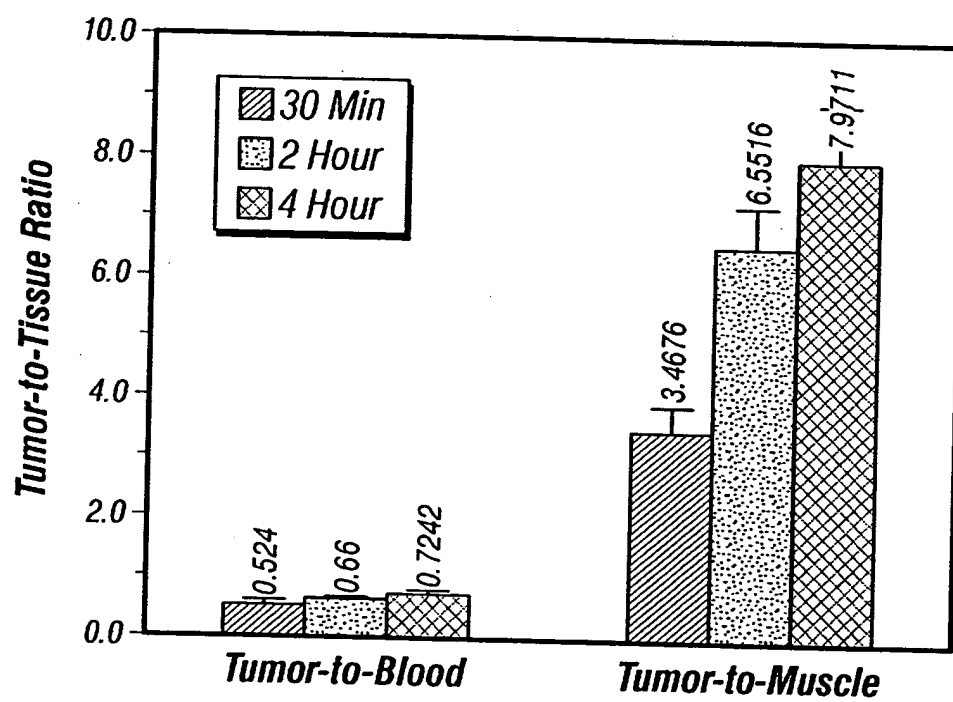


FIG. 23

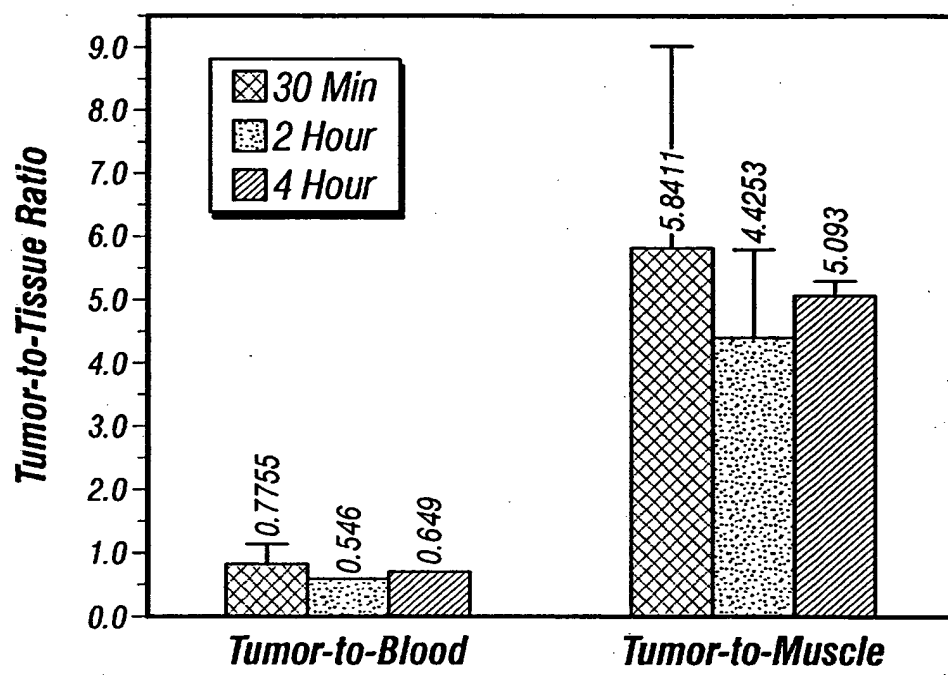


FIG. 24

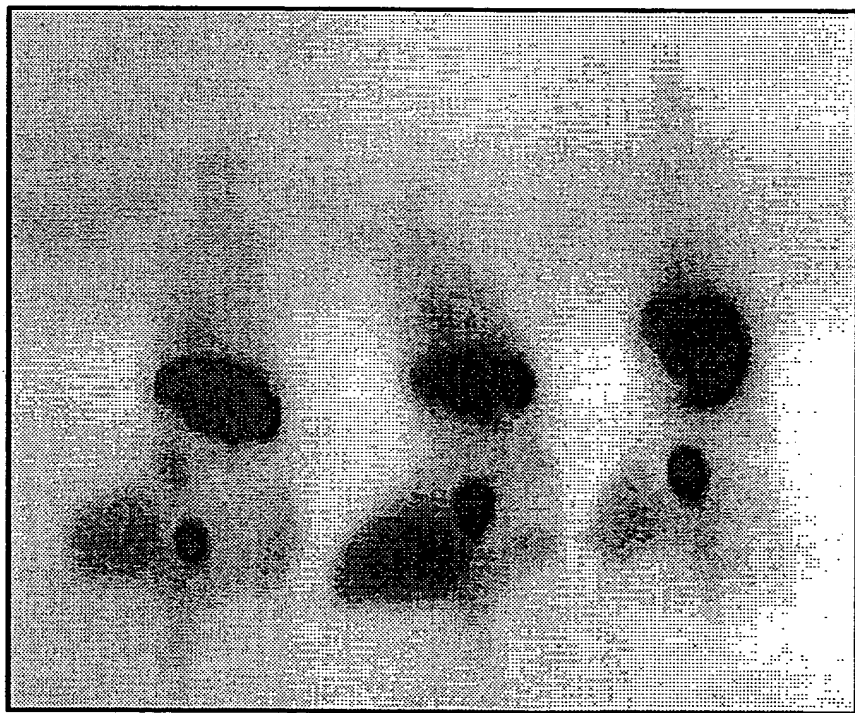


FIG. 25

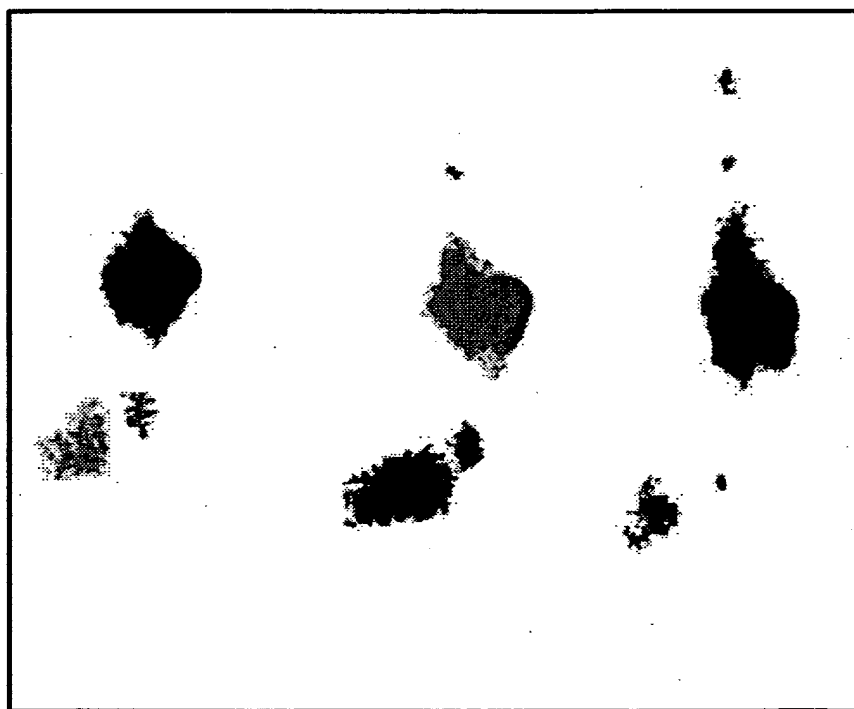


FIG. 26

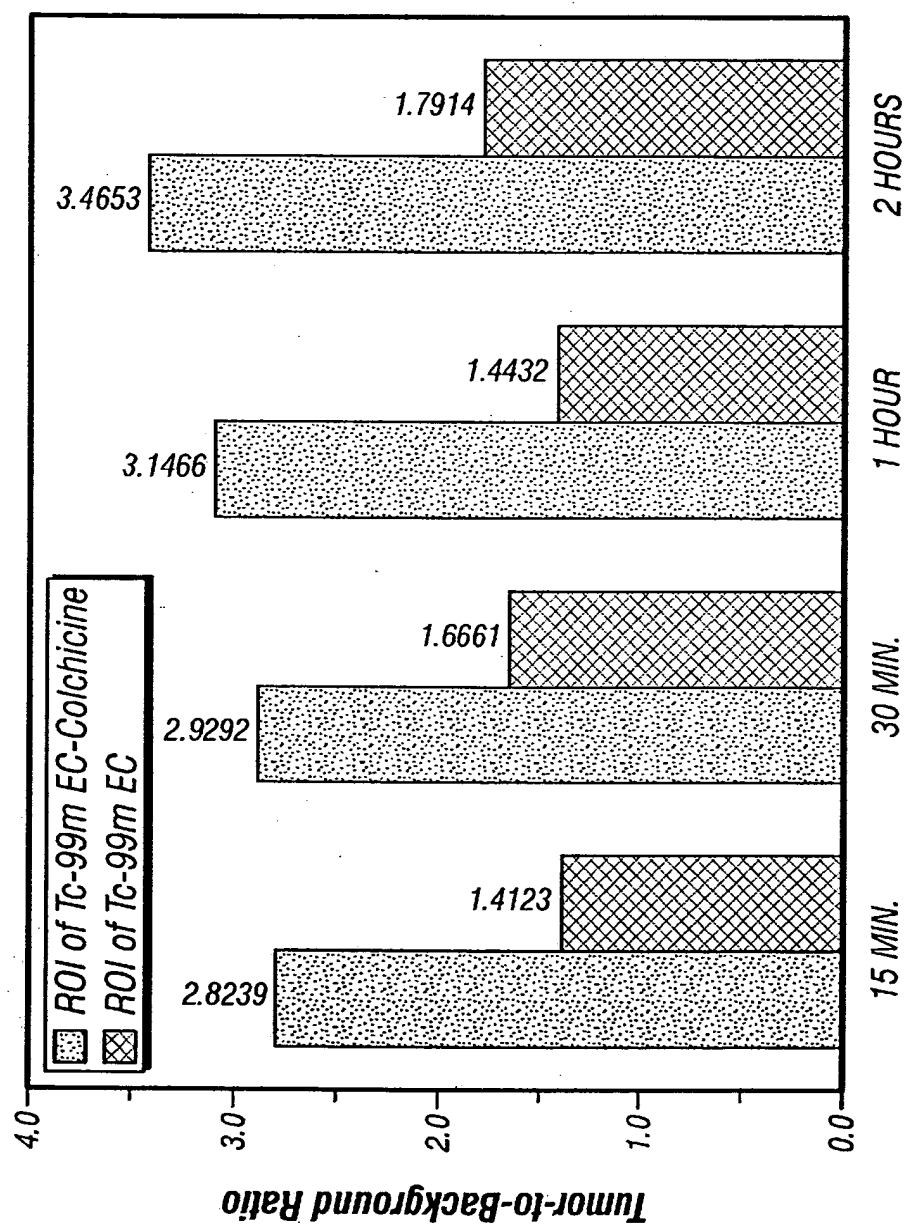


FIG. 27

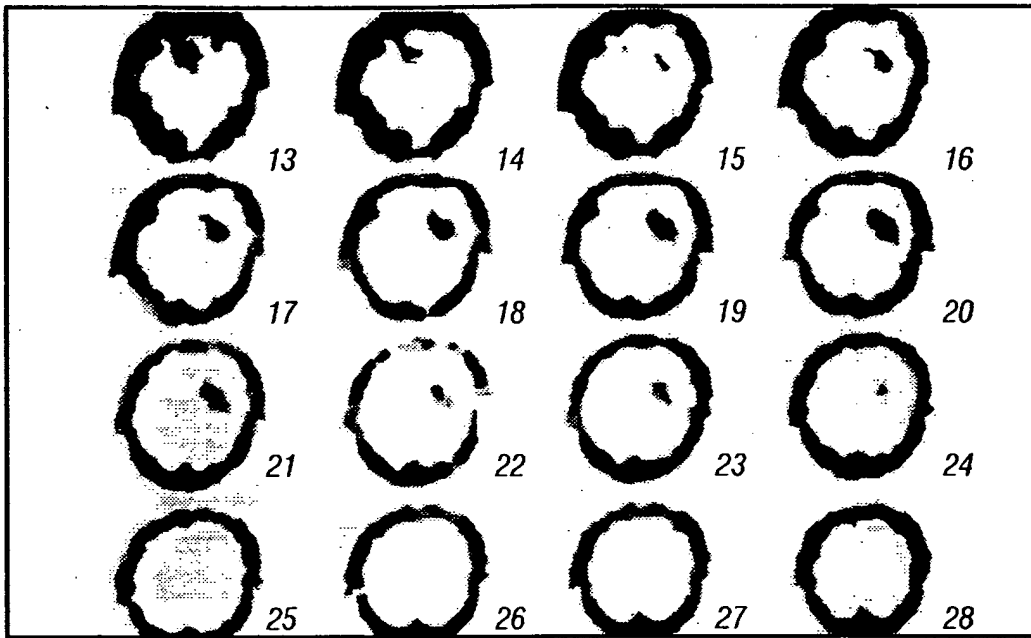


FIG. 28



FIG. 29

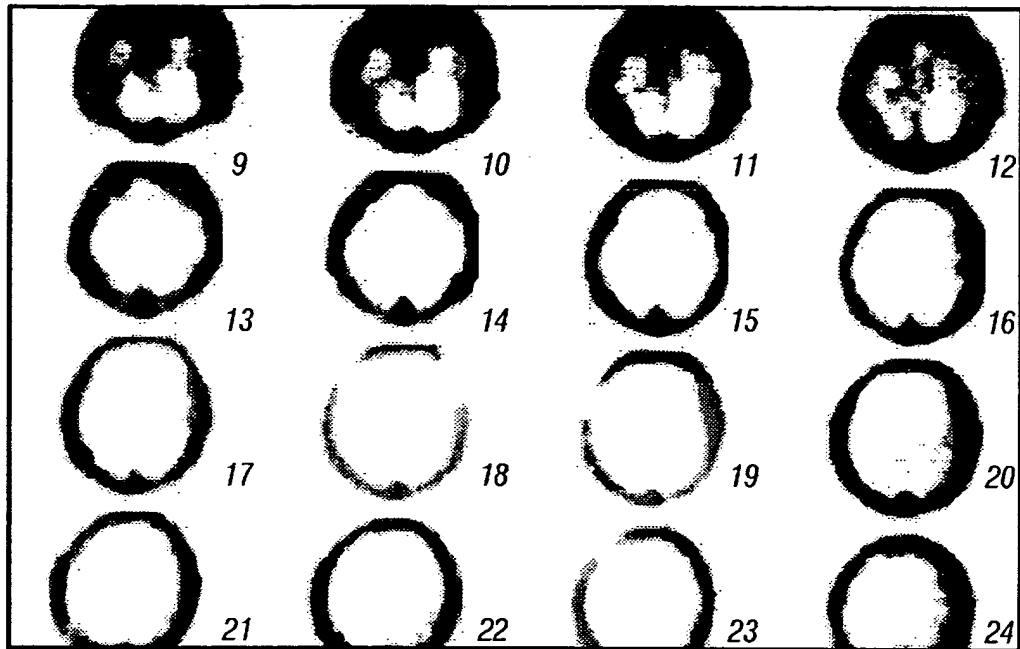


FIG. 30

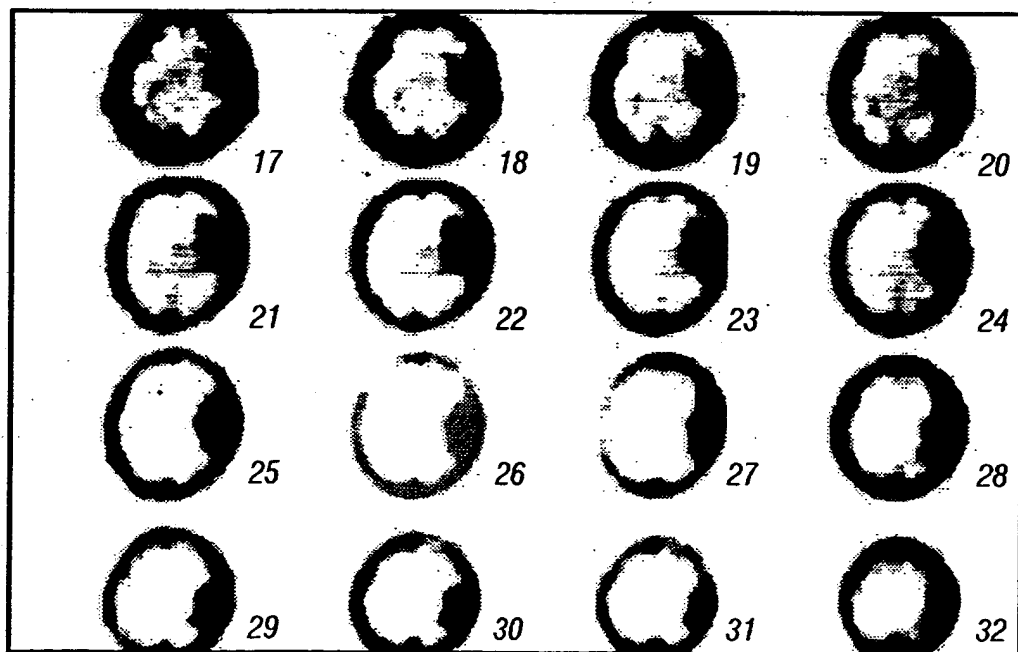


FIG. 31

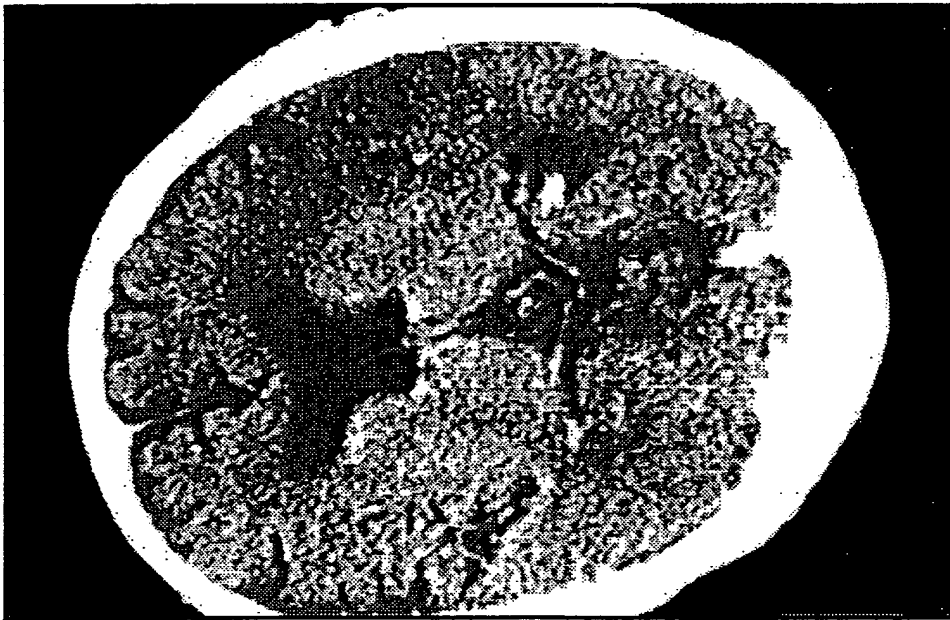


FIG. 32

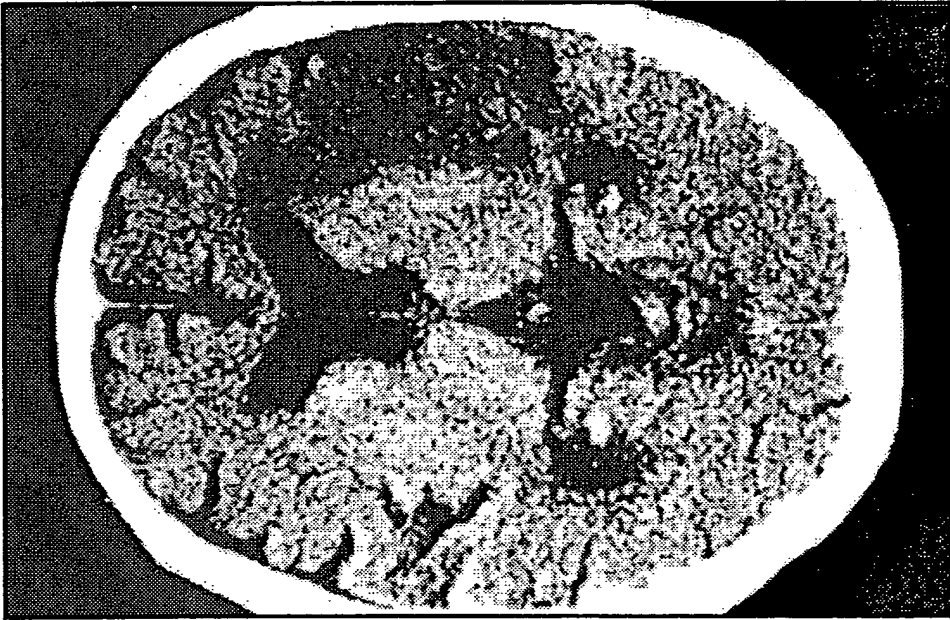


FIG. 33

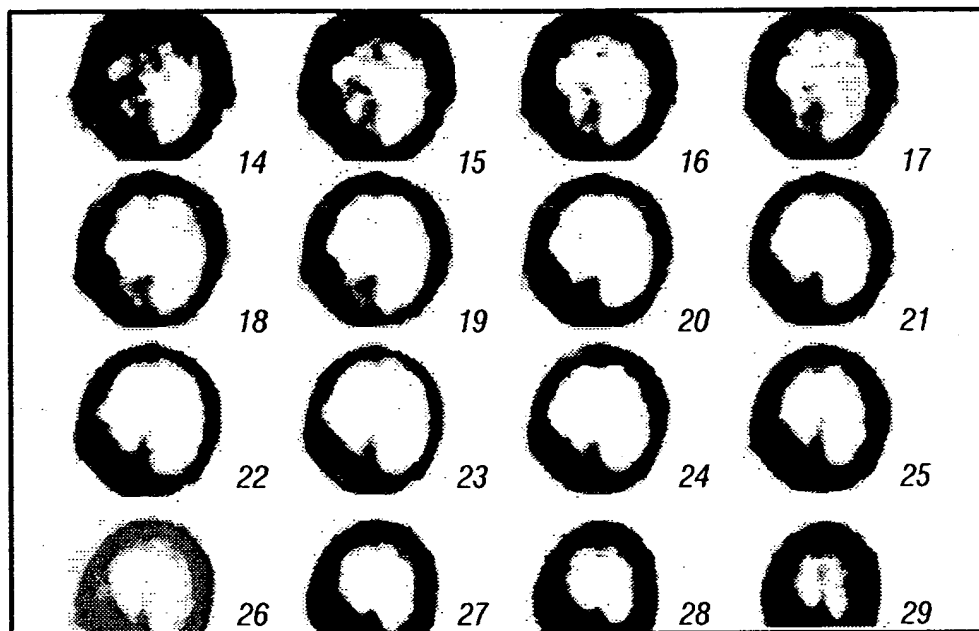


FIG. 34

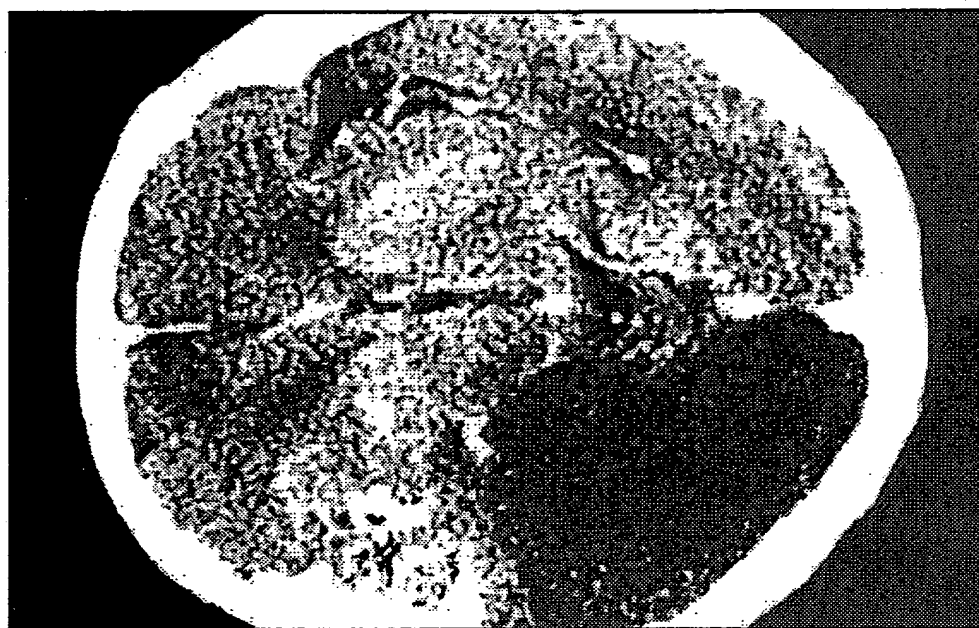


FIG. 35

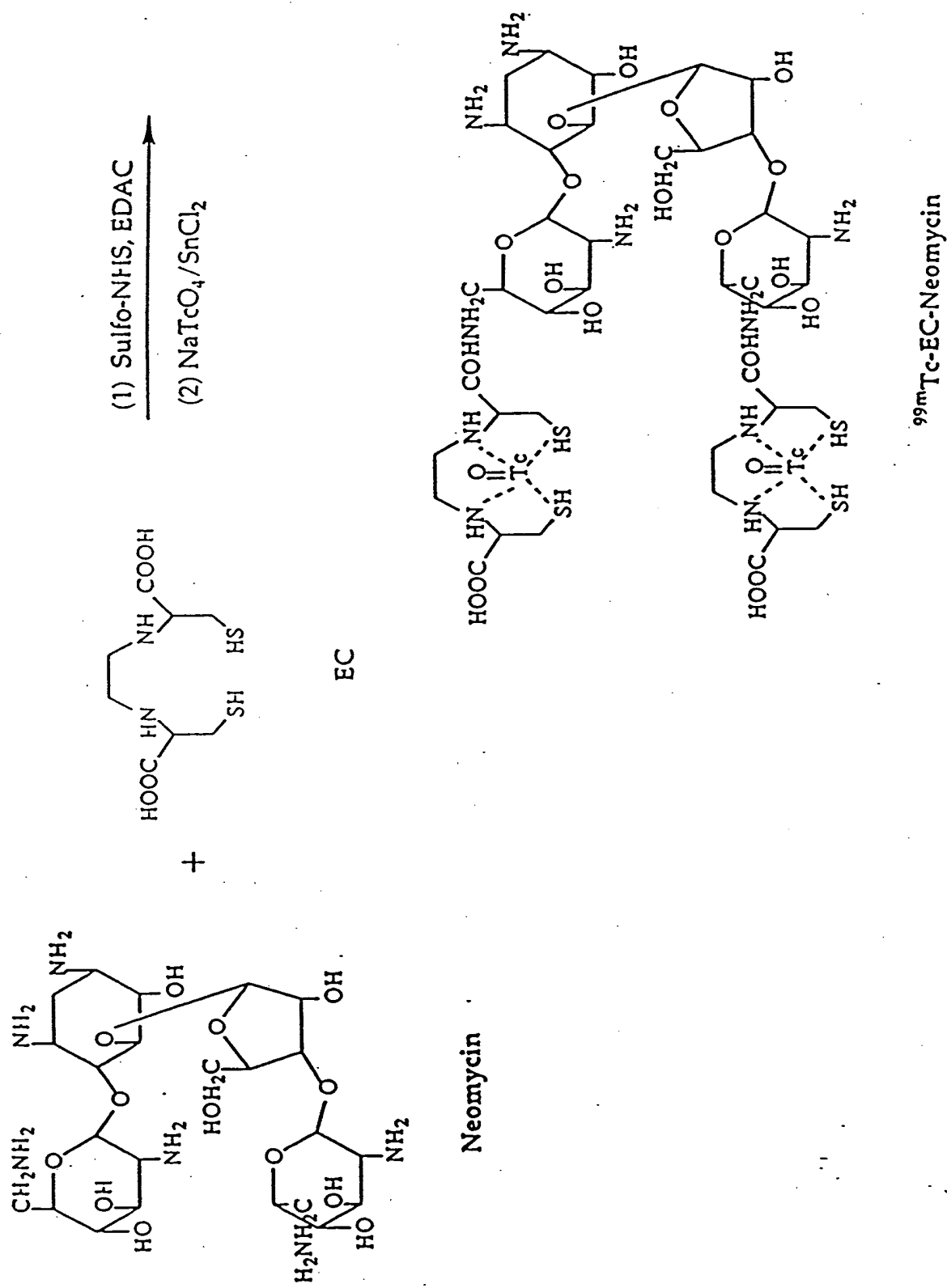
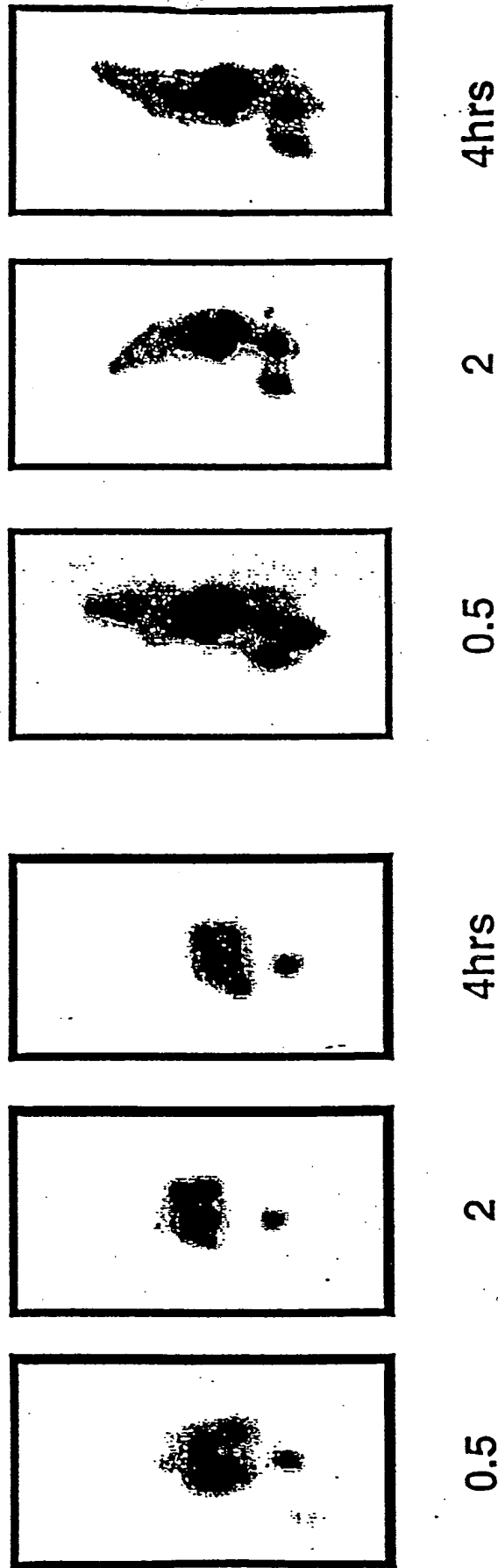


FIG. 36

Synthetic scheme of $^{99\text{m}}\text{Tc-EC-neomycin}$.

$^{99m}\text{Tc-EC}$

$^{99m}\text{Tc-EC-Neomycin}$



Planar image of breast tumor-bearing rats after administration of $^{99m}\text{Tc-EC}$ and $^{99m}\text{Tc-EC-Neomycin}$ ($100\mu\text{Ci/rat, iv.}$) showed that the tumor could be well visualized from 0.5-4 hours postinjection.

FIG. 37A
Scintigraphic image of breast tumor-bearing rats after administration of $^{99m}\text{Tc-EC}$ and $^{99m}\text{Tc-EC-Neomycin}$ ($100\mu\text{Ci/rat, iv.}$) showed that the tumor could be well visualized from 0.5-4 hours postinjection.

WOO IN JA 753717-1163 2000 WONKWANG UNIV HOSP
SCINTIMAMMOGRAPHY EC-NEO

LT LAT-2H

RT LAT-2H

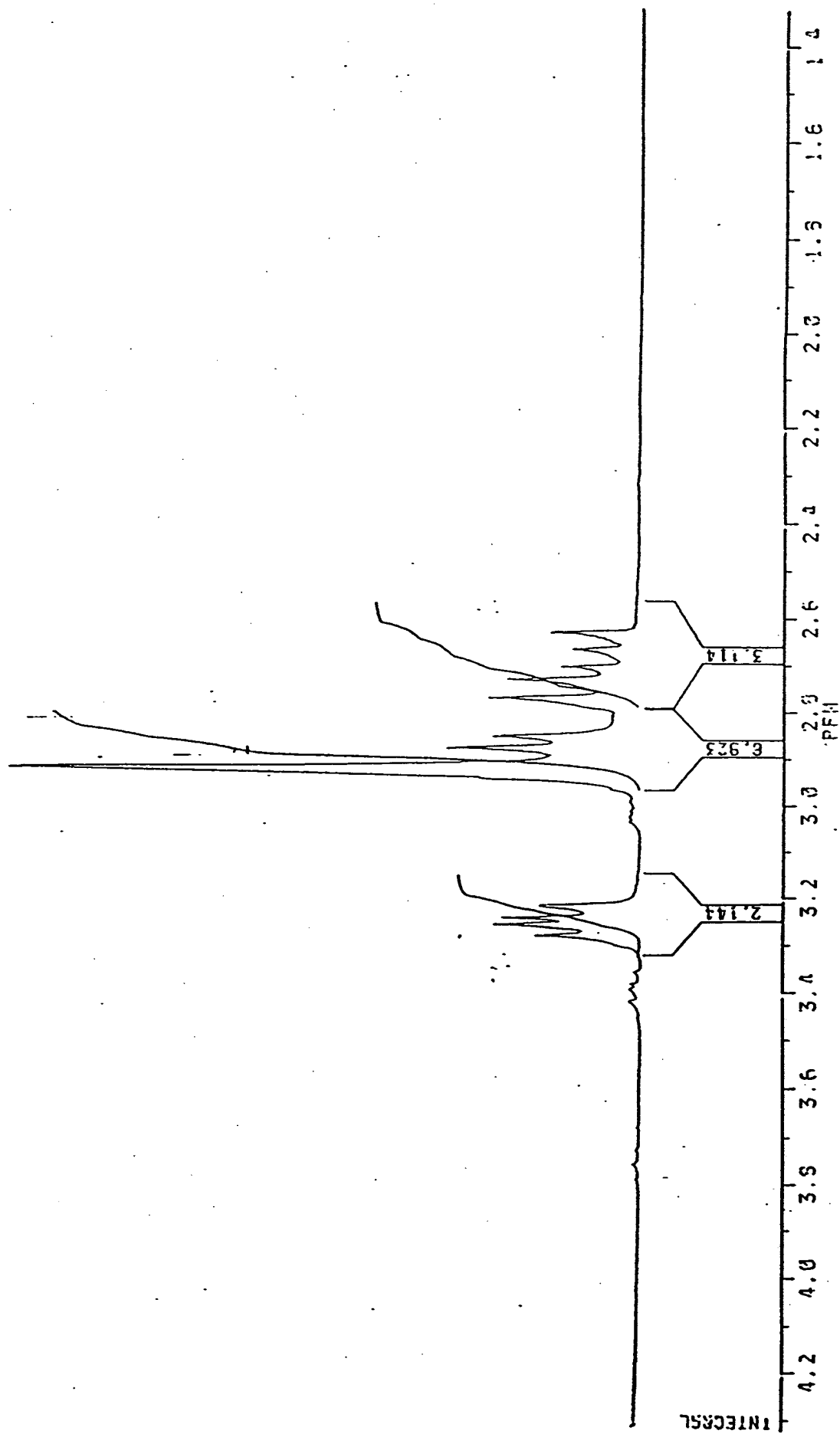
LT LAT-2H

RT LAT-2H

FIG. 37B

Scintimammography with ^{99m}Tc -EC- neomycin (30 mCi, iv.) of a breast cancer patient. Images taken two hours post-injection.

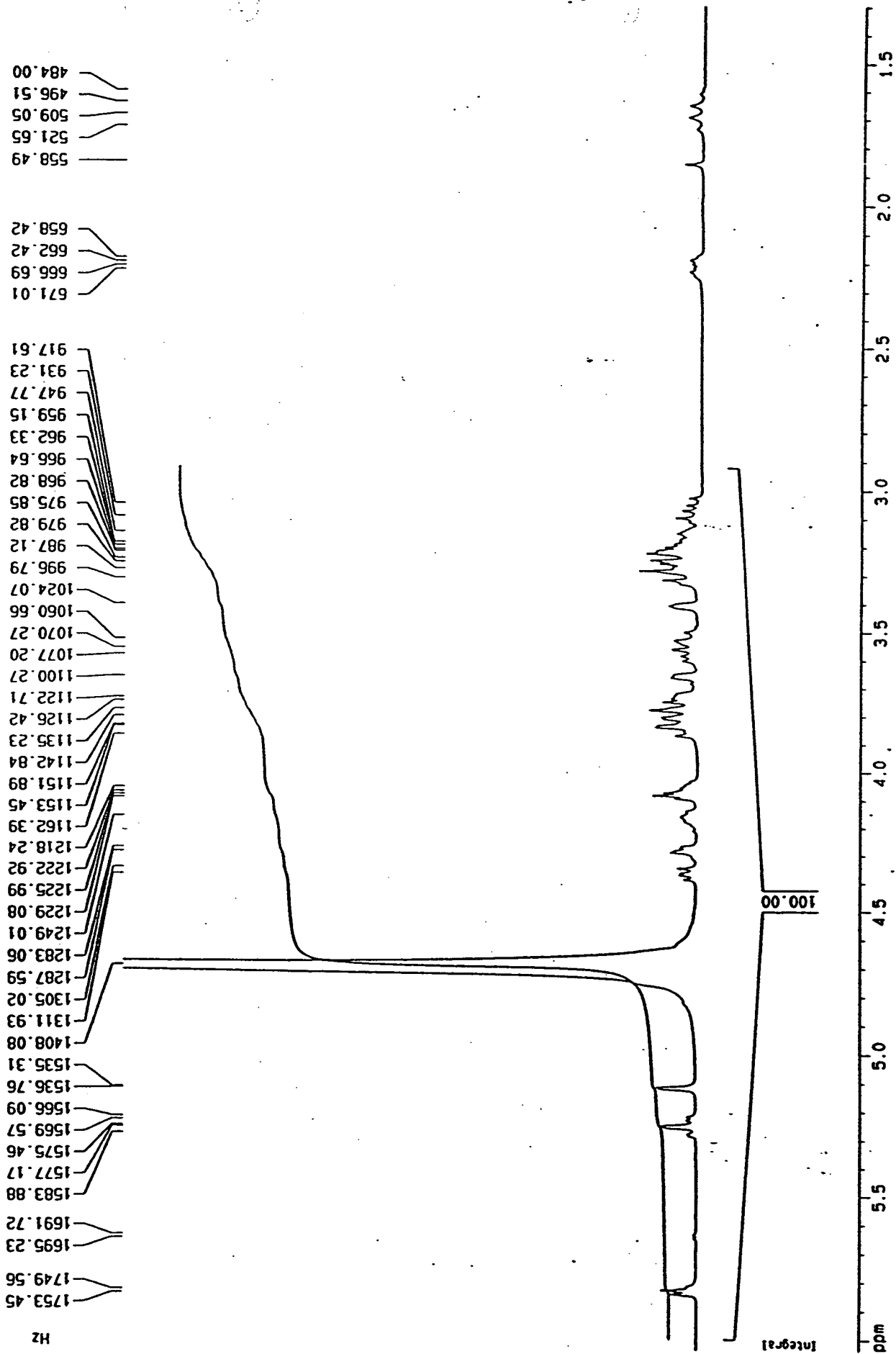
EC.



^1H -NMR of EC.

FIG. 38A

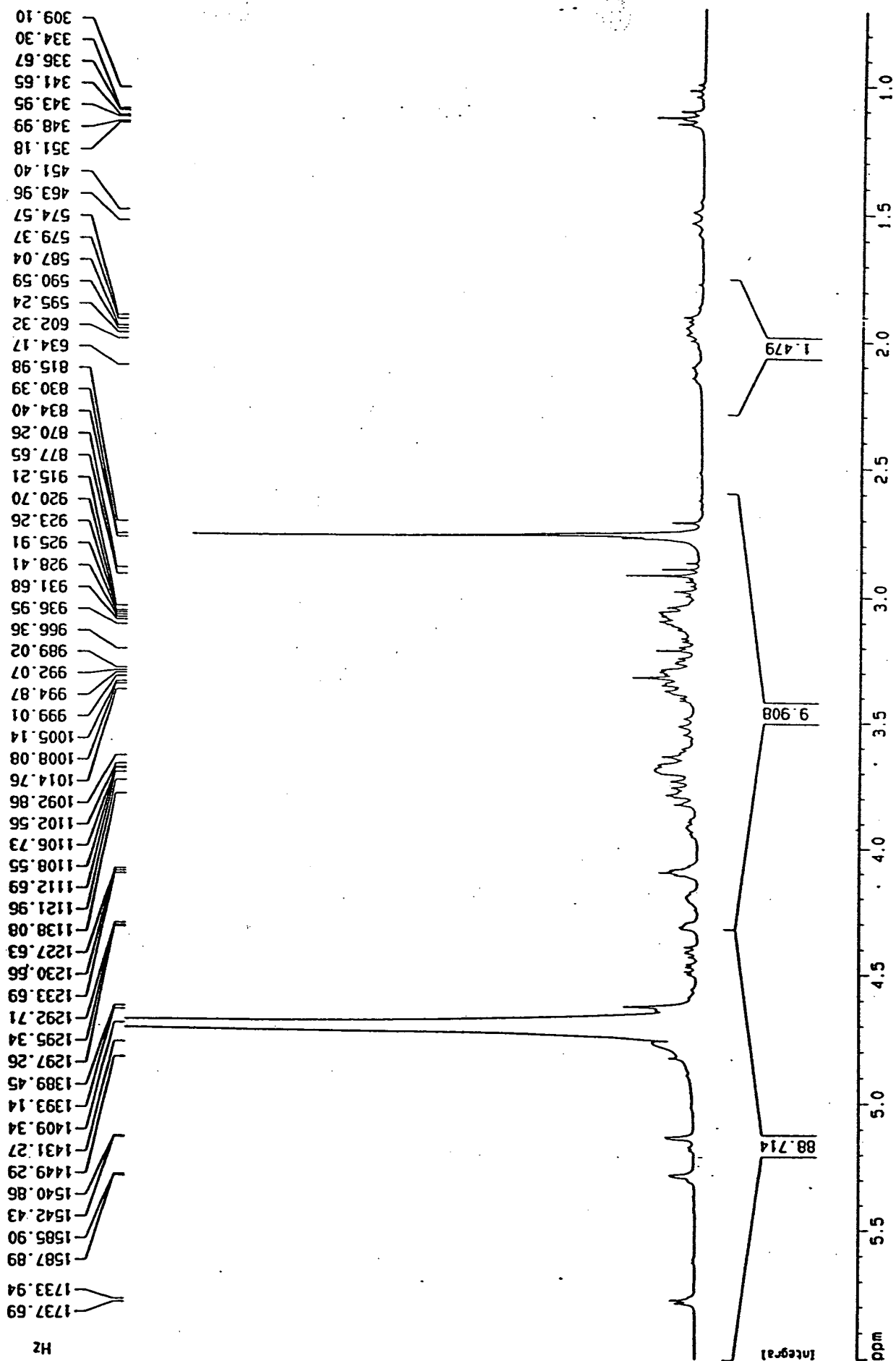
Neomycin



^1H -NMR of neomycin.

FIG. 38B

EC-Neomycin



¹H-NMR of EC-neomycin.

FIG. 38C

UV Wavelength Scan of EC

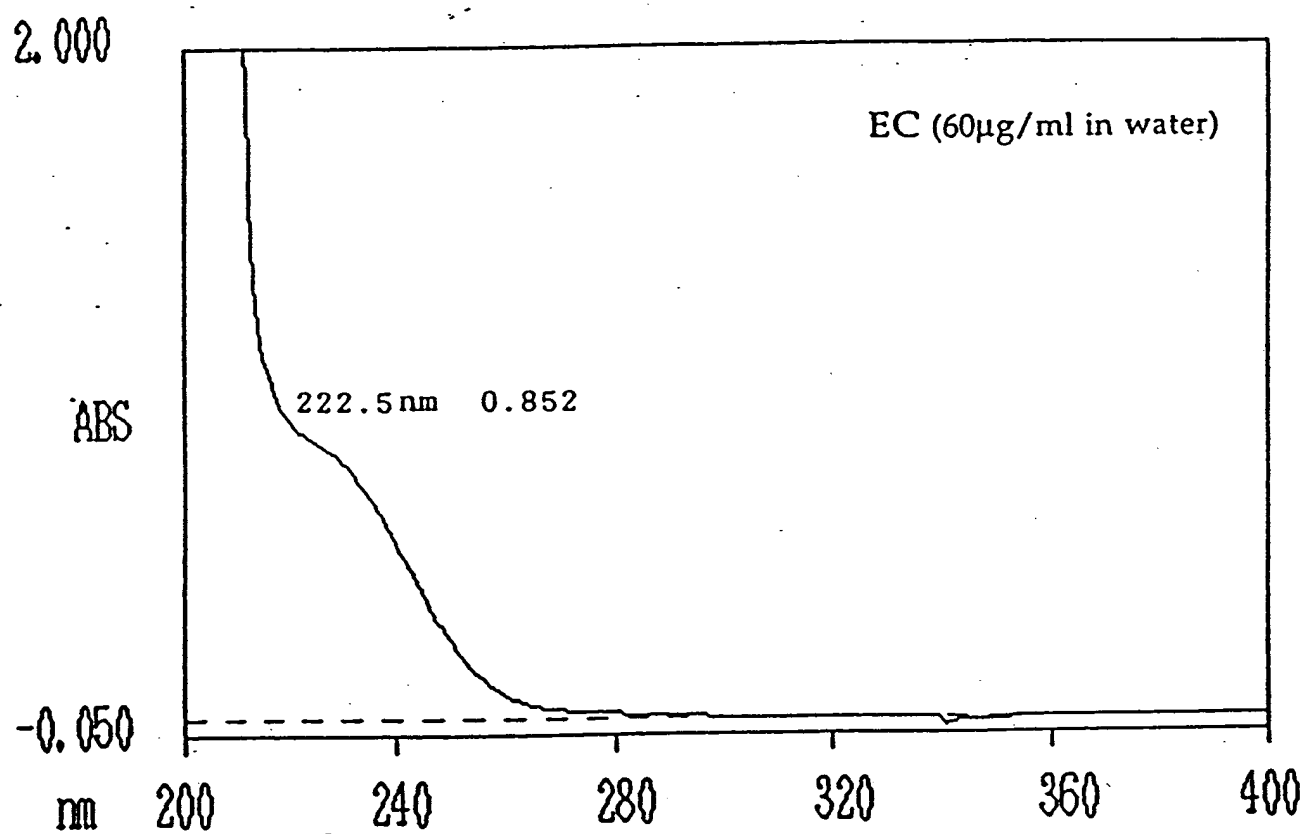


FIG. 40A

UV wavelength scan of EC.

UV Wavelength Scan of Neomycin

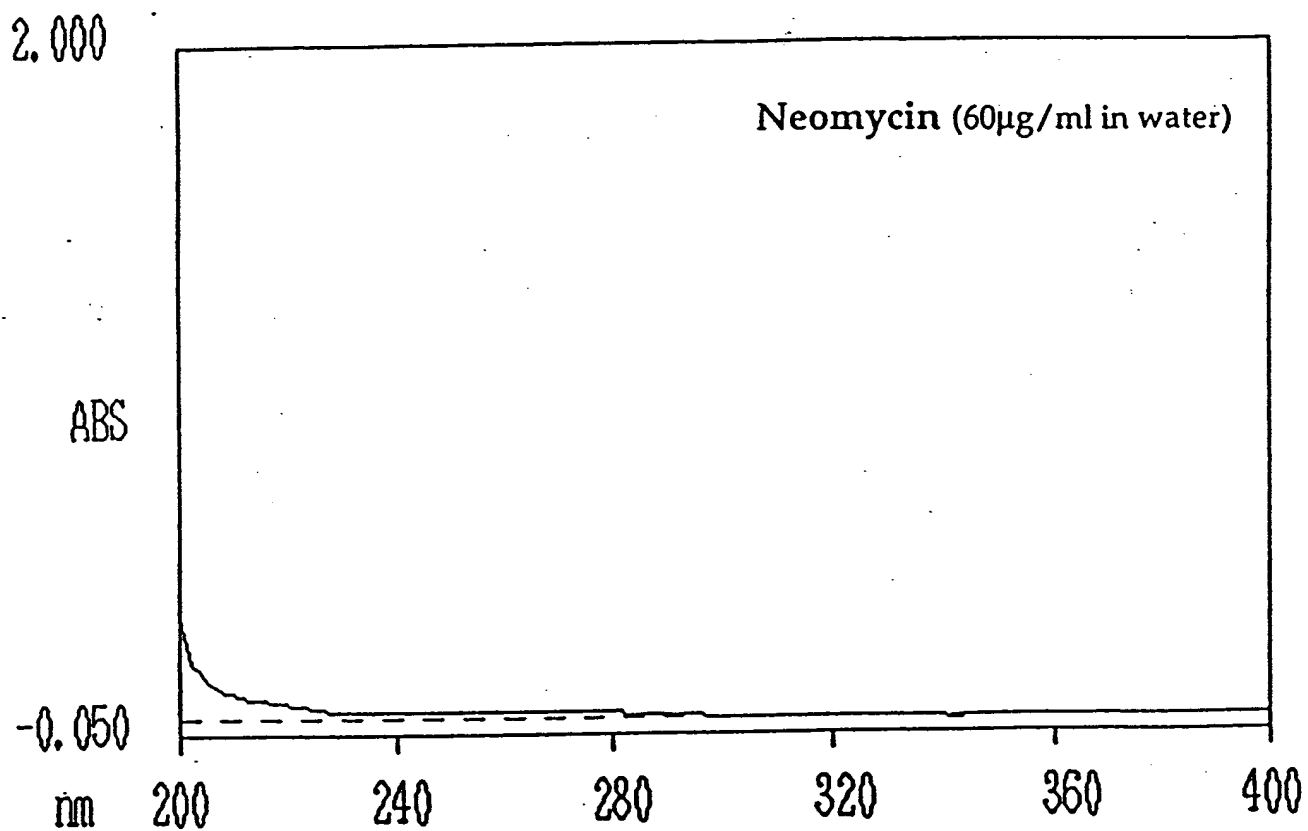


FIG. 40B

UV wavelength scan of neomycin.

UV Wavelength Scan of EC-Neomycin

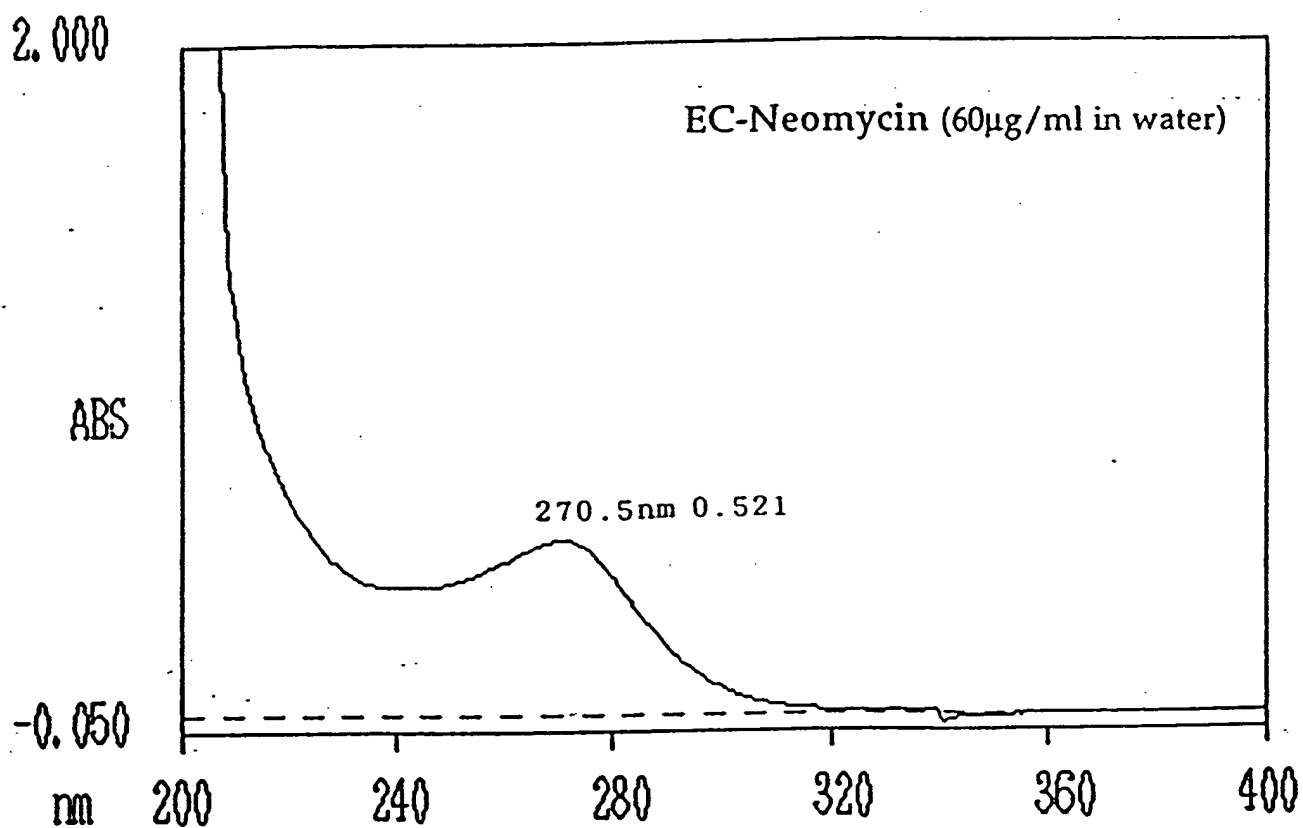


FIG. 40C

UV wavelength scan of EC-neomycin.

SUMMARY REPORT

EC-NEOMYCIN 30mg + EC

Tc-99m

METHANOL-AMMONIUM ACETATE

Date: Feb 03 2000

Start time: 12:45

Accum time: 00:03:01

Data File:

Plate: 1 Lane: 1

Elect Resolution: NORMAL

(Amp. Range: 0 - 2047)

Rf Calculations: Origin: 0.00 cm

Solvent Front: 20.00 cm

Integration Parameters: Auto Integration

Peak slope: 1.0

Min width: 0.1

Min %: 2.0

Total Count Region: 0.00cm to 20.00cm

Total Counts: 48360

Total CPM: 16030

Reg. #	Start (cm)	Stop (cm)	Center (cm)	Rf	Region Counts	Region CPM	% of Tot Reg	% of Tot Cnt
1	6.50	14.90	10.57	0.53	45000	14920	100.00	93.05
TOTAL					45000	14920	100.00	93.05

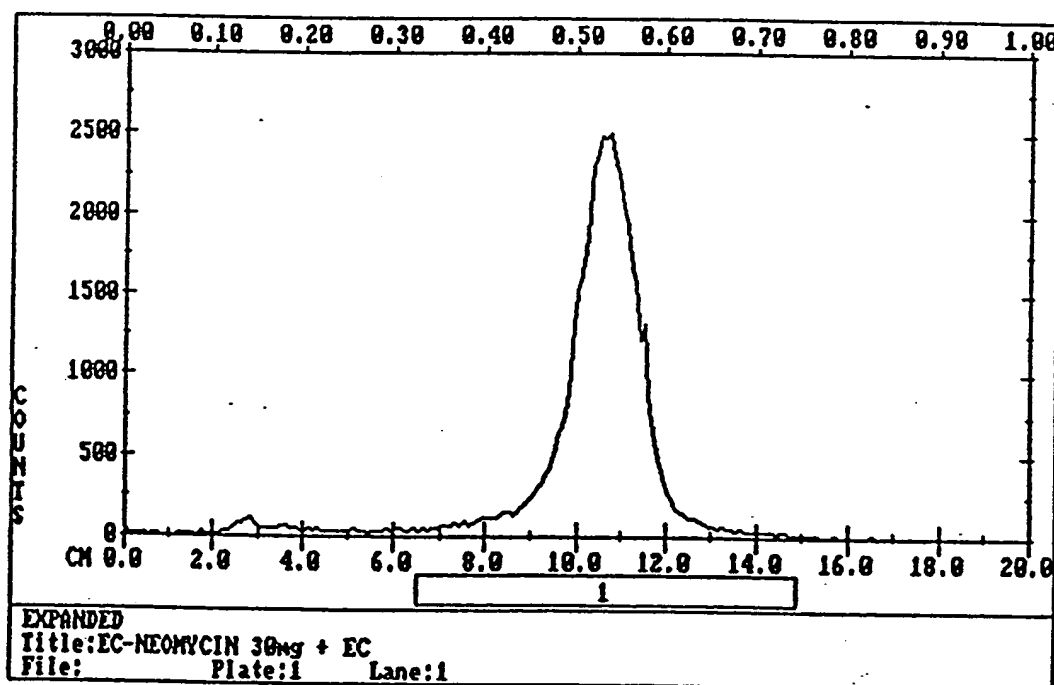


FIG. 41

Radio-TLC analysis of ^{99m}Tc-EC-neomycin.

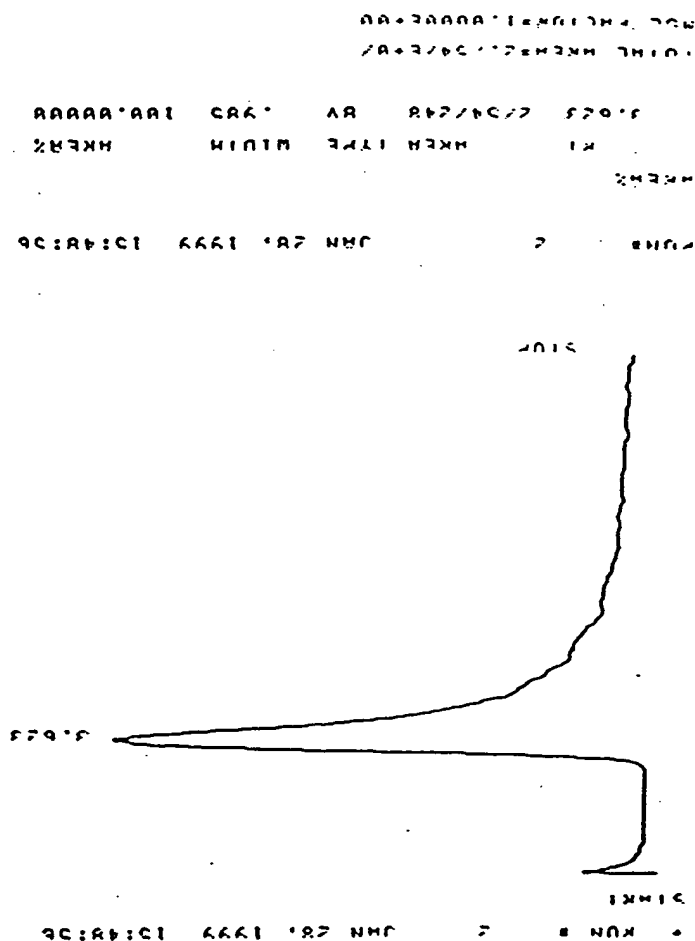
Column: Bio-Rad Carbohydrate, Aminex HPX-87C, 250x4mm

Eluent: H₂O

Flow Rate: 0.4ml/min

Detector: Radiochemical

Temp: 85.0°C



HPLC analysis of ^{99m}Tc -EC-neomycin (radioactive detector).

^{99m}Tc-EC-NEO

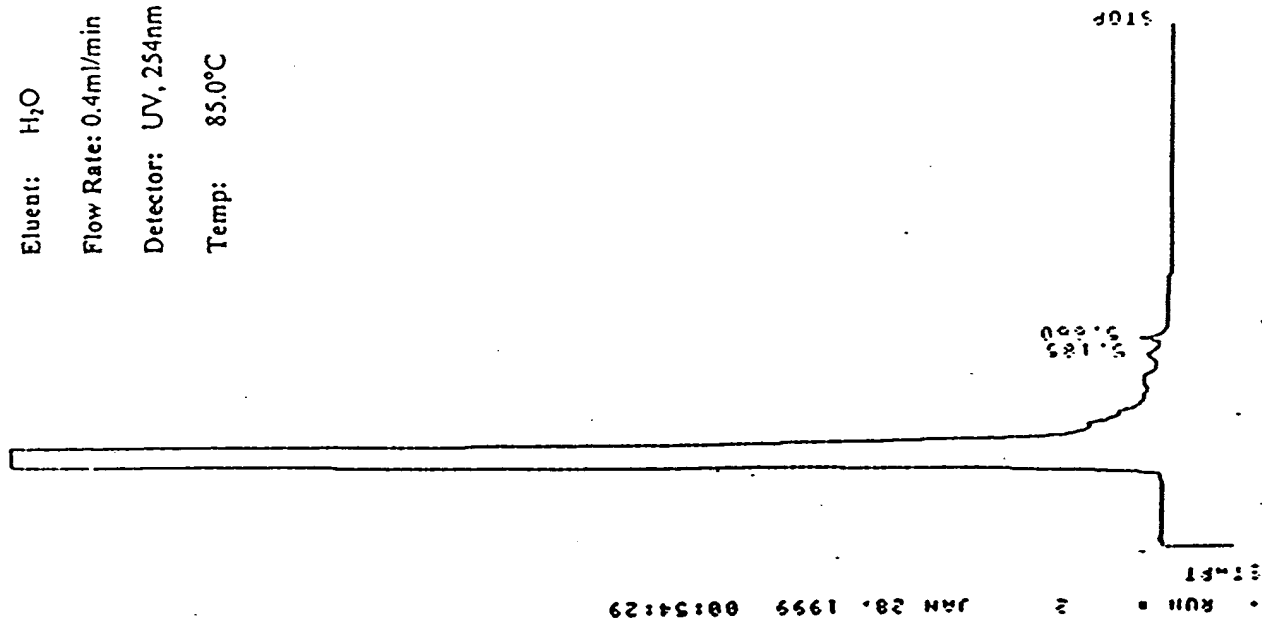
Column: Bio-Rad Carbohydrate, Aminex HPLX-87C, 250x4mm

Eluent: H₂O

Flow Rate: 0.4ml/min

Detector: UV, 254nm

Temp: 85.0°C



RT	AREA	TYPE	WIDTH	AREA%
5.183	255506480	SPK	1.498	99.71165
5.185	392604	BV	1.265	1.5126
5.680	355901	VB	1.132	1.13712
TOTAL AREA=2.5955E+08				
NET FACTOR=1.0000E+00				

¹⁸F-FDG

Column: Bio-Rad Carbohydrate,
Aminex HPX-87C, 250x4mm

Eluent: H₂O

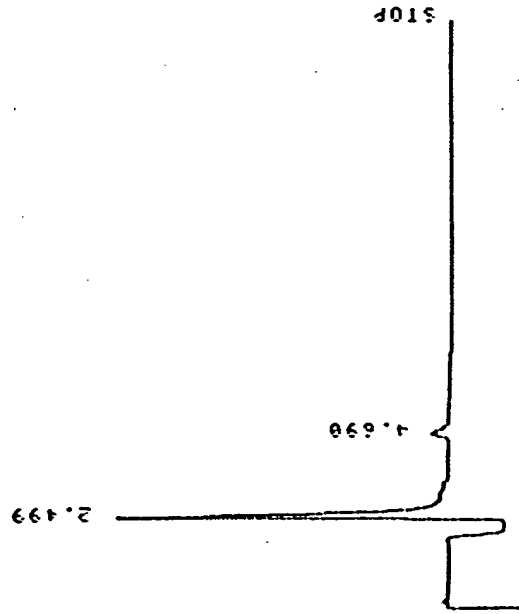
Flow Rate: 0.4ml/min

Detector: UV, 254nm

Temp: 85.0°C

RUN # 1 JAN 28, 1999 00:37:02

RUN # 1 JAN 28, 1999 00:37:02



DATE 1/28/99
JAN 28, 1999 00:16:15
• CH1 SP 1.5 @
• AT 2 @
• THRESH 2 @
• LIST: LIST
PEAK CAPACITY: 1244
ZERO = 0. -11.179
AT 2 = 3
CH1 SP = 0.5
NR REJ = 0
THRESH = 2
FW NO = 0.04

FIG. 45 HPLC analysis of ¹⁸F-FDG (UV 254 nm).

% of Drug Uptake in Lung Cancer Cell Line (A549)

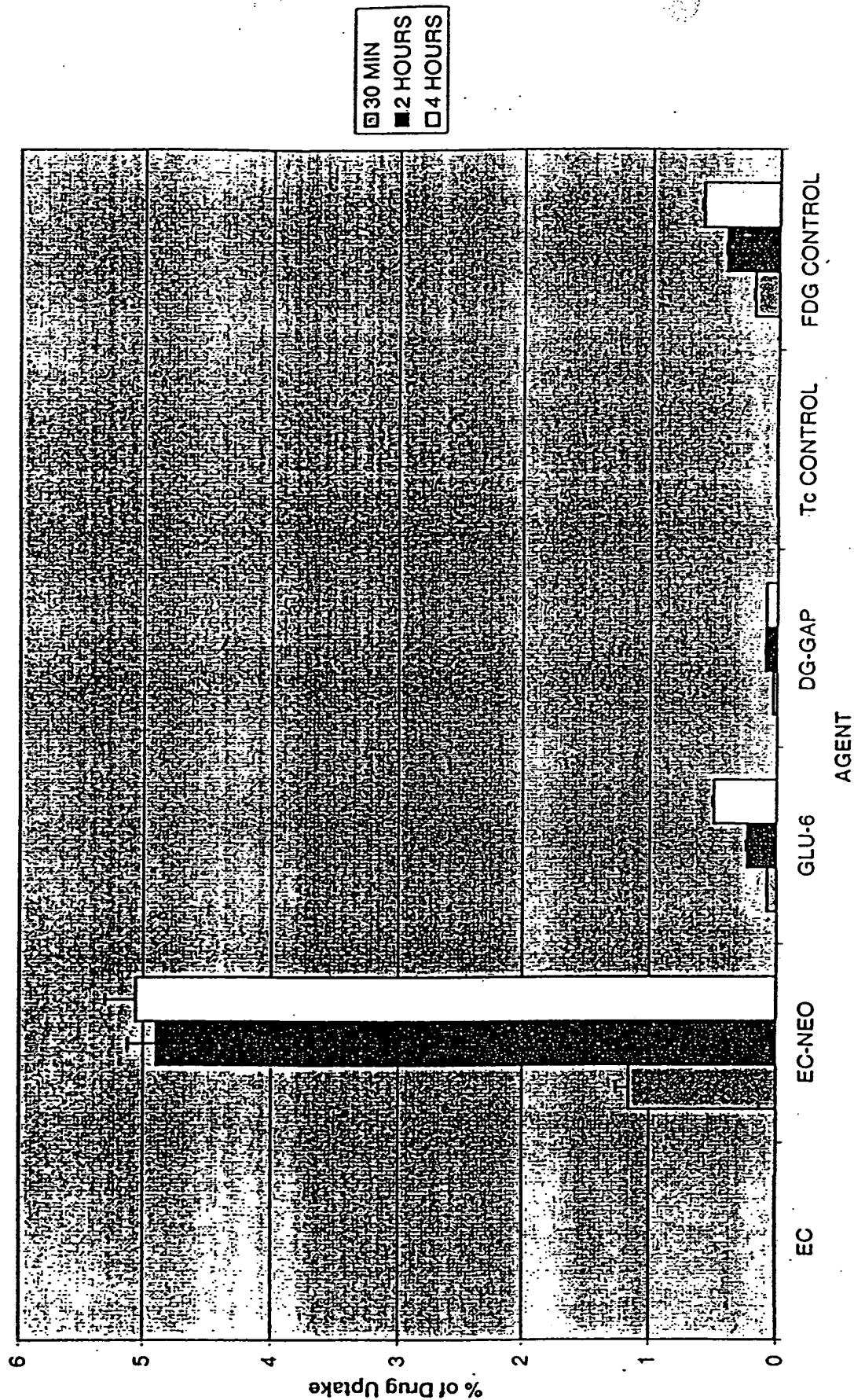
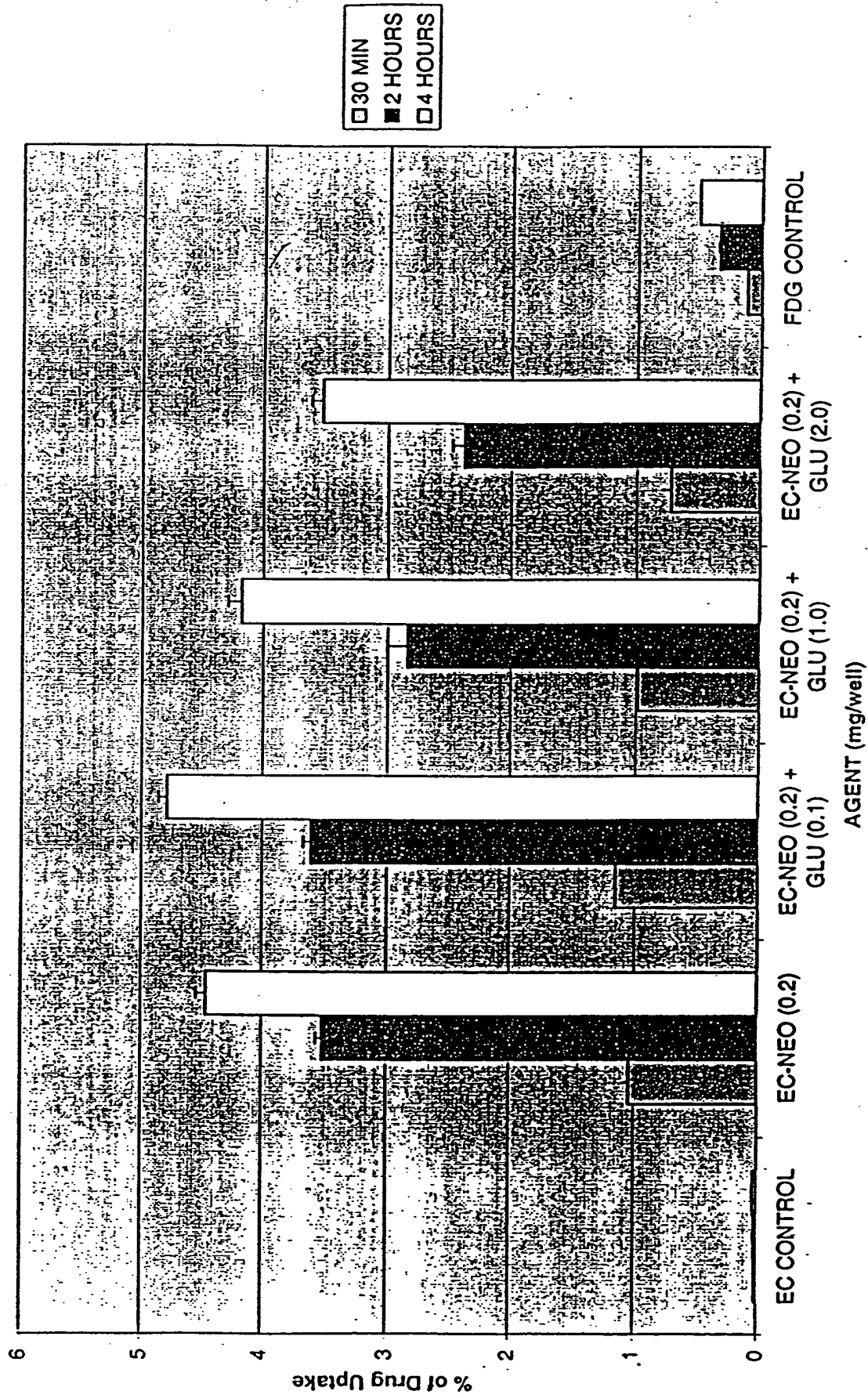


FIG. 46

In vitro cellular uptake assay of a series of ^{99m}Tc -EC-drug conjugates in lung cancer cell line. ^{99m}Tc -EC- neomycin showed

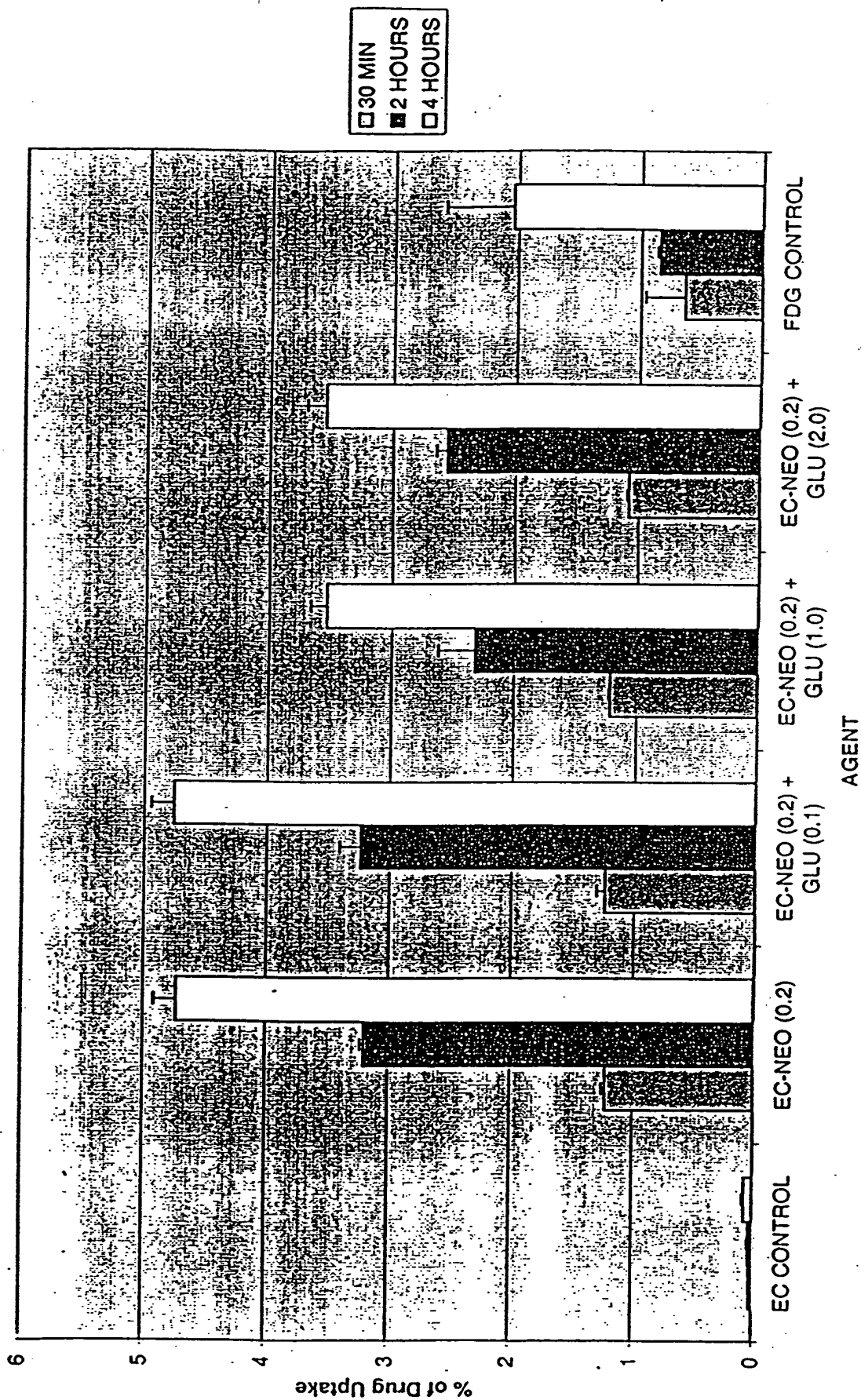
% of Drug Uptake in Human Lung Cancer Cell Line (A549)



Effect of glucose on cellular (A549) uptake of ^{99m}Tc -EC- neomycin and ^{18}F -FDG.

FIG. 47

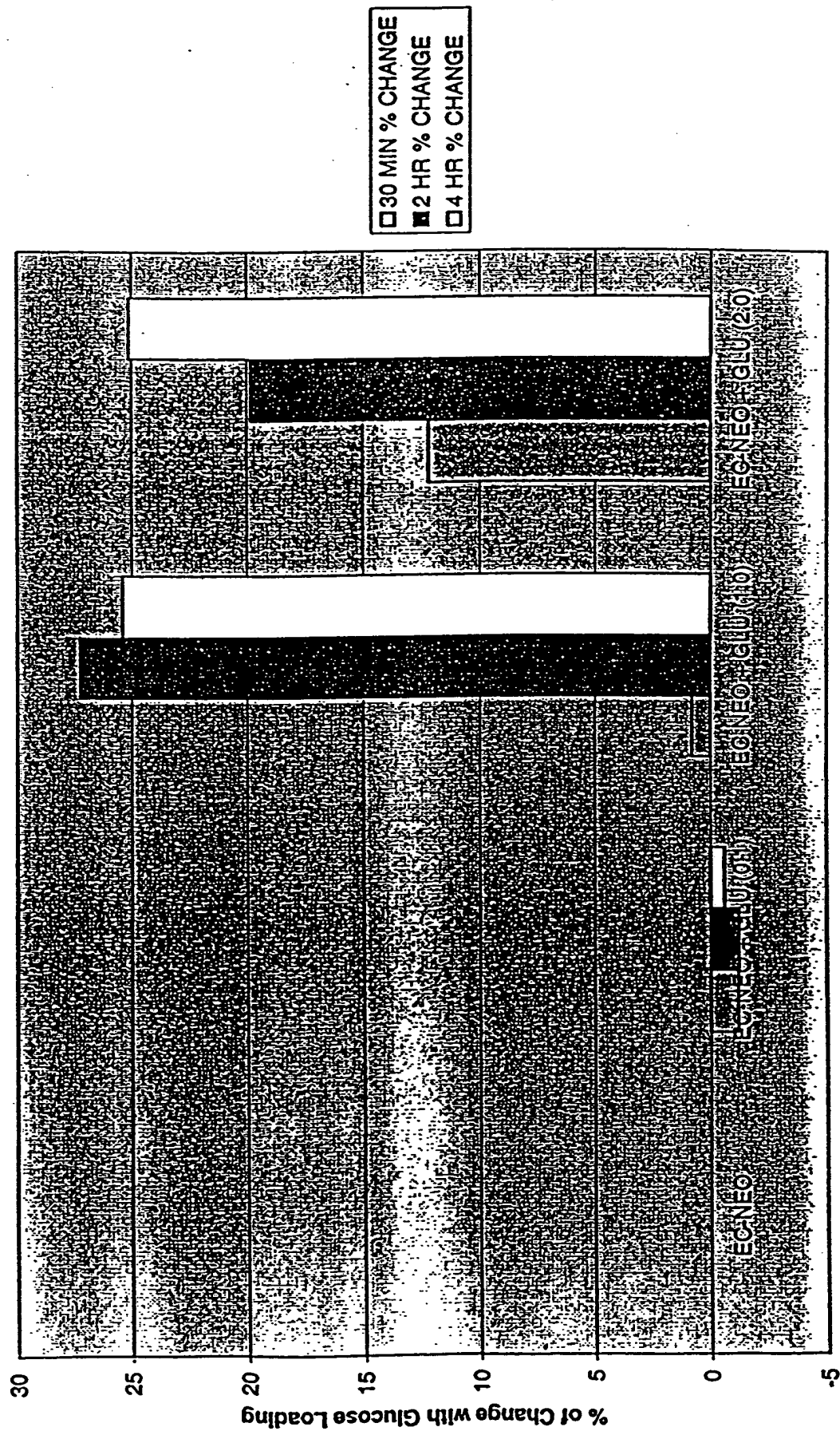
% of Drug Uptake in Human Lung Cancer Cell Line (H1299)



Effect of glucose on cellular (H1299) uptake of ^{99m}Tc -EC-

FIG. 48A

Effects of Glucose Loading on ^{99m}Tc -EC-Neomycin in Human Lung Cancer Cell Line (H1299)



AGENT (dose)

FIG. 48B

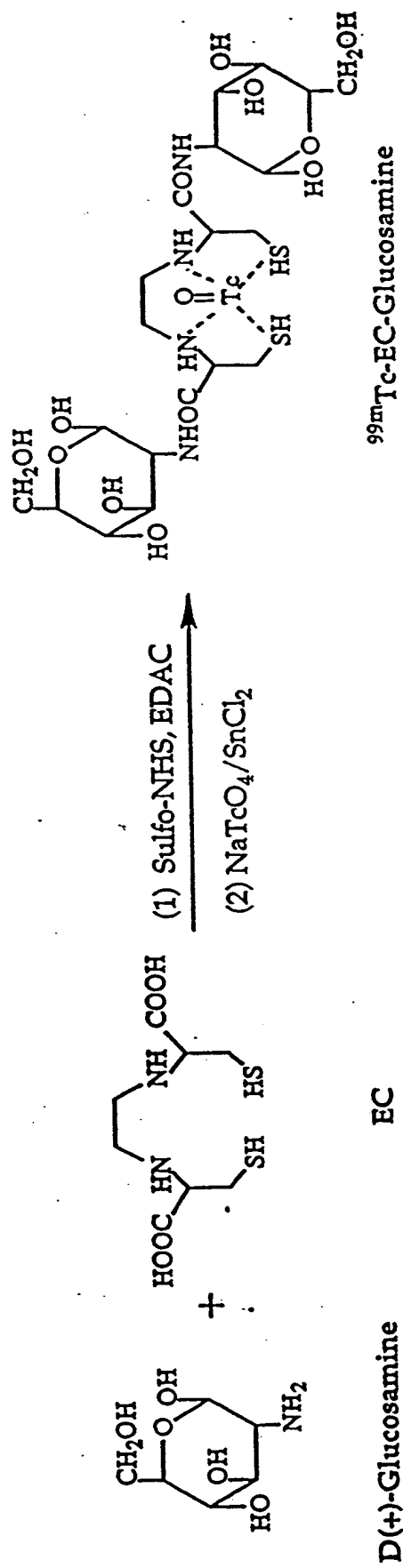
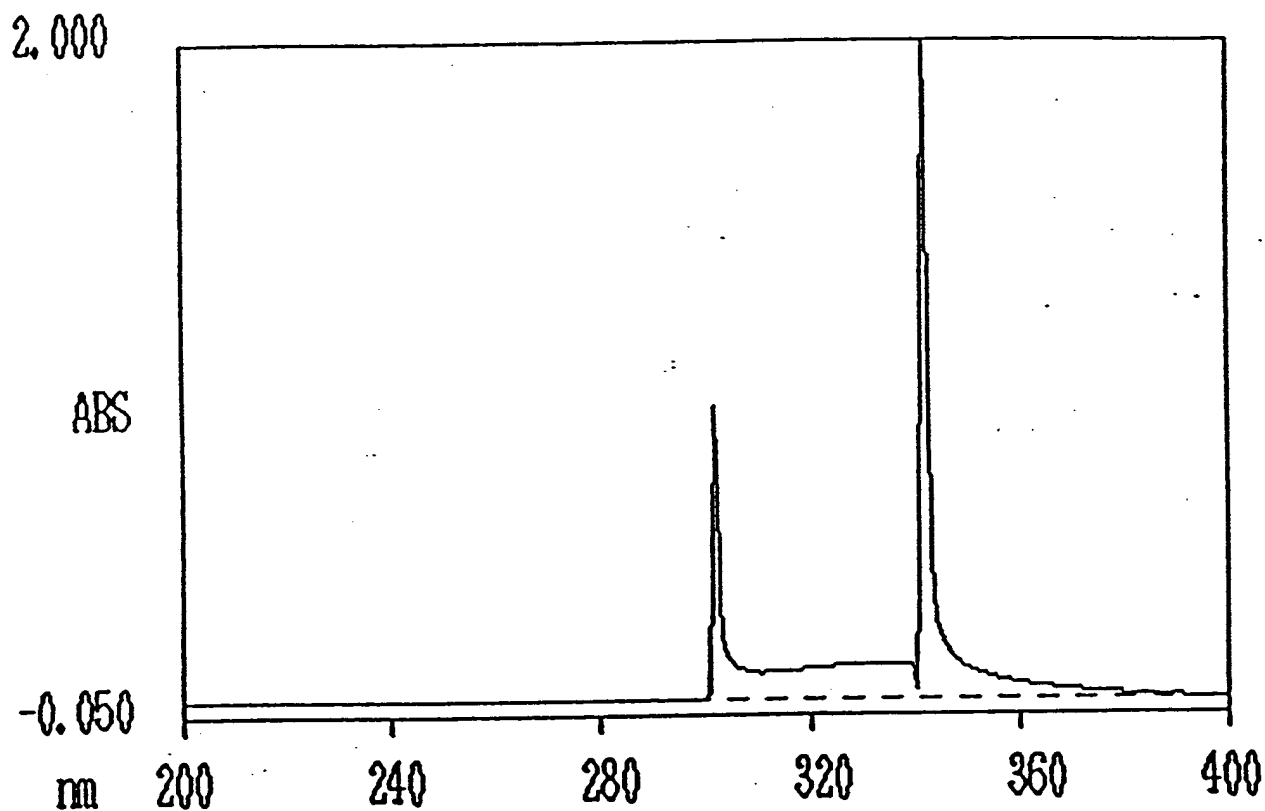


FIG. 49 Synthesis of $^{99\text{m}}\text{Tc-EC-Glucosamine}$

Hexokinase Assay of Glucose

WAVELENGTH SCAN/0

03/01/00 14:41



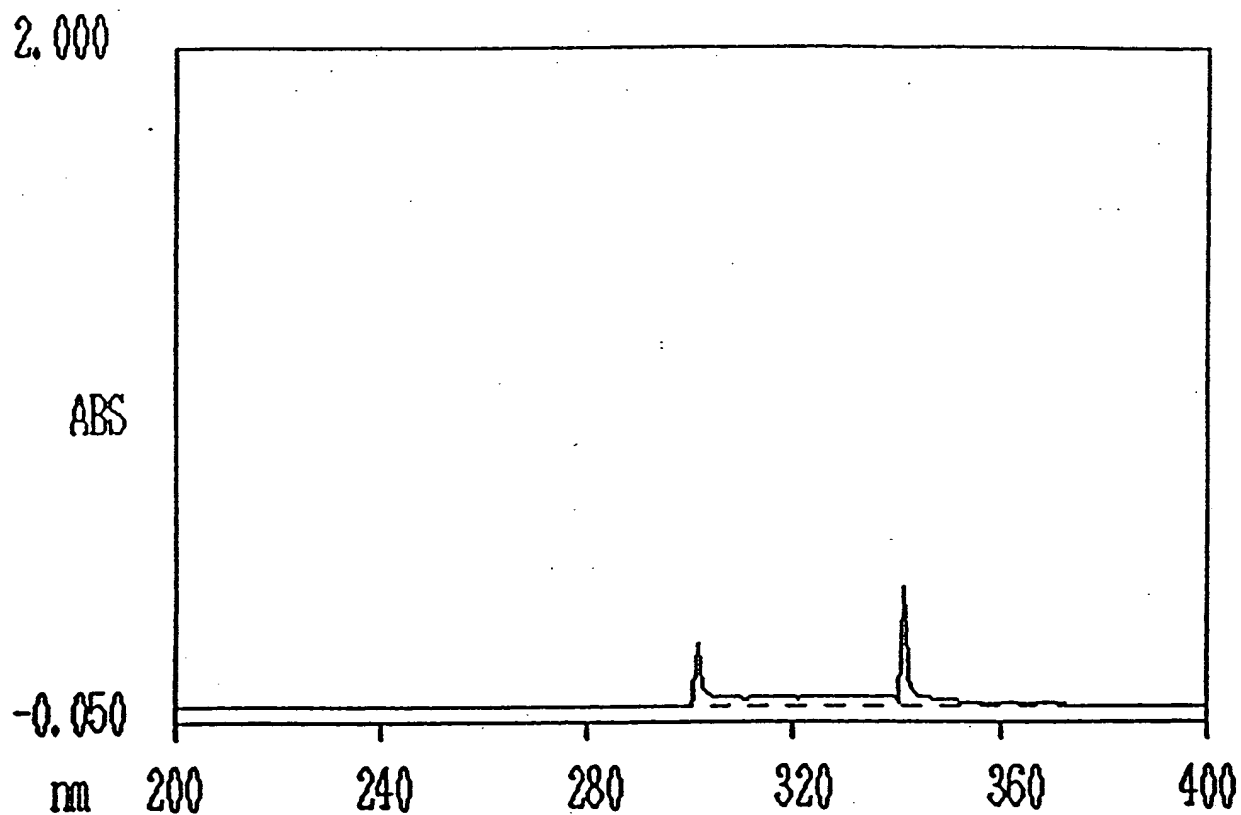
301.5 nm	0.889 ABS
342.0 nm	2.044 ABS

FIG. 50

Hexokinase Assay of Glucosamine

WAVELENGTH SCAN/0

03/01/00 14:50



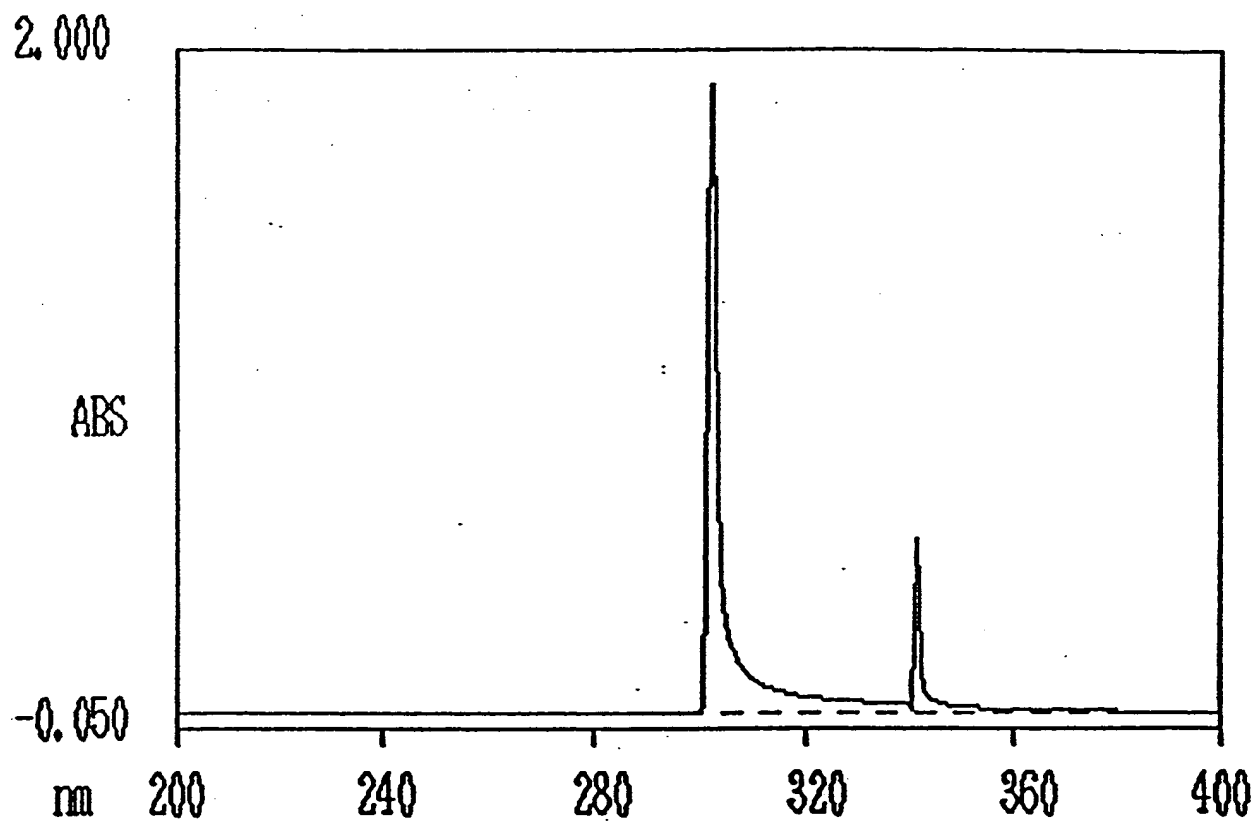
301.5 nm 0.193 ABS
341.5 nm 0.360 ABS

FIG. 51

Hexokinase Assay of EC-Glucosamine

WAVELENGTH SCAN/0

03/01/00 14:45



302.5 nm 1.897 ABS
341.5 nm 0.523 ABS

FIG. 52

Hexokinase Assay of EC-GAP-Glucosamine

WAVELENGTH SCAN/0

03/01/00 15:37

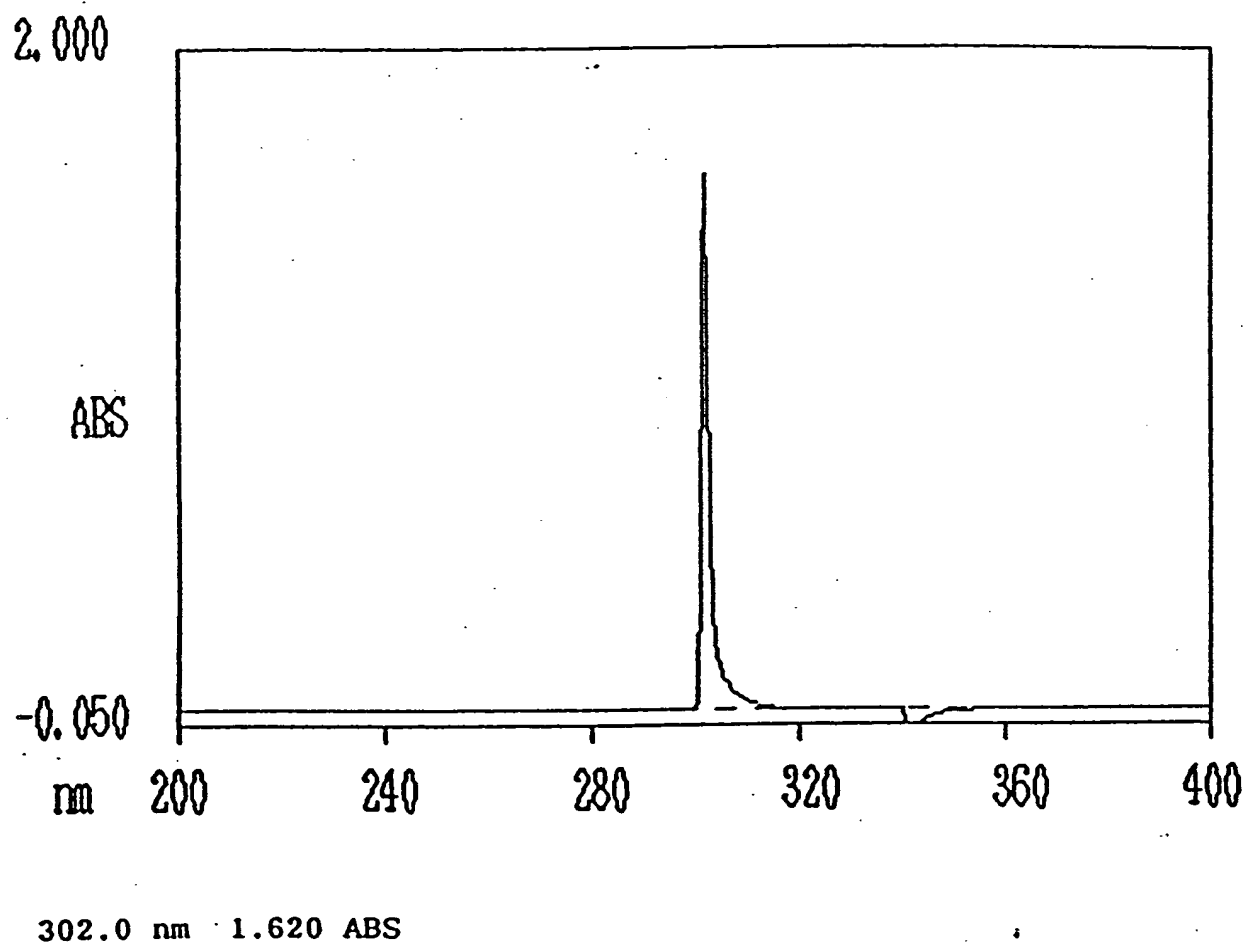


FIG. 53

In Vitro Cellular Uptake of ^{99m}Tc -EC in Human Lung Cancer Cell Line (A549)

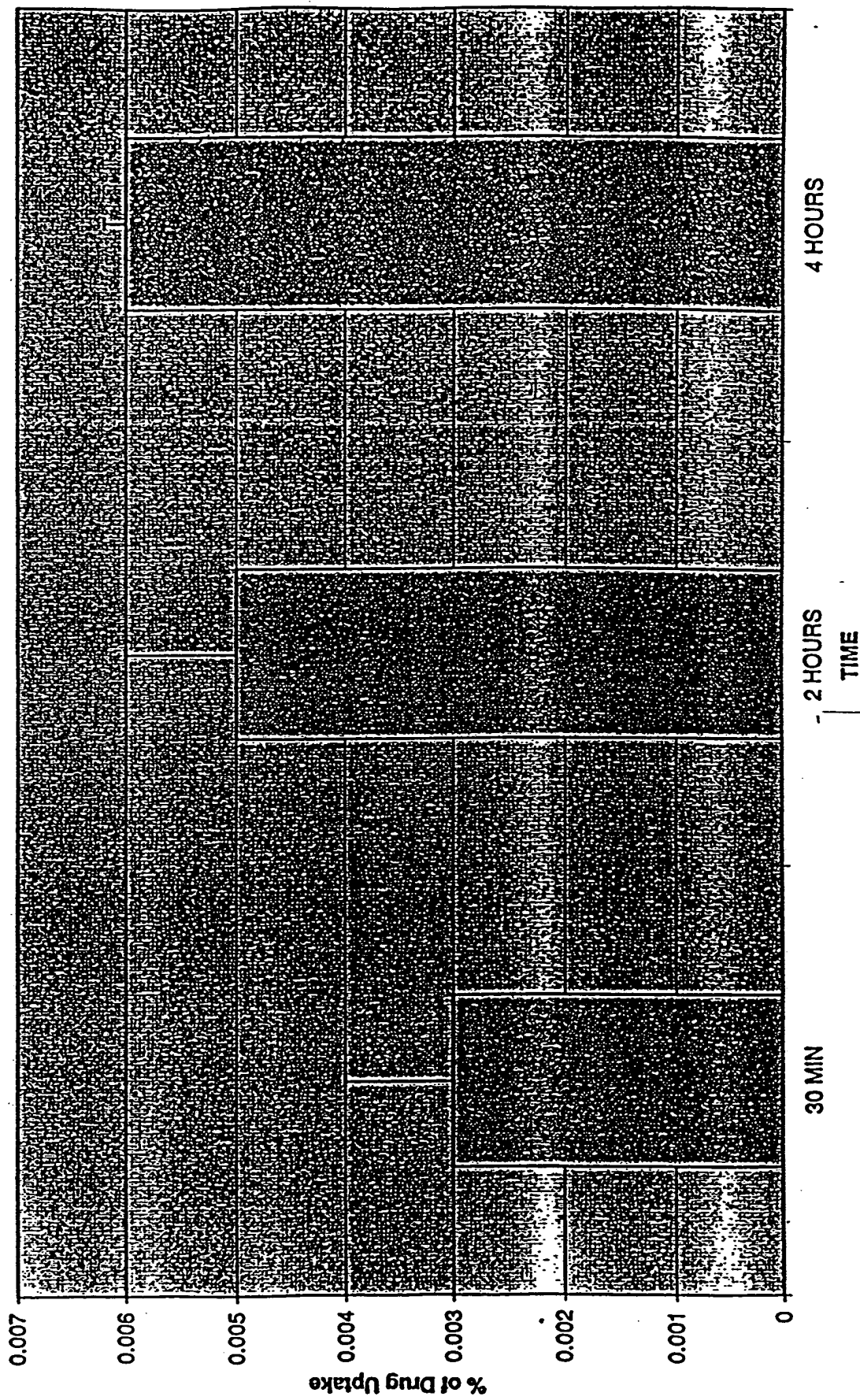


FIG. 55A

In Vitro Cellular Uptake of ^{99m}Tc -EC-DG-GAP in Human Lung Cancer Cell Line (A549)

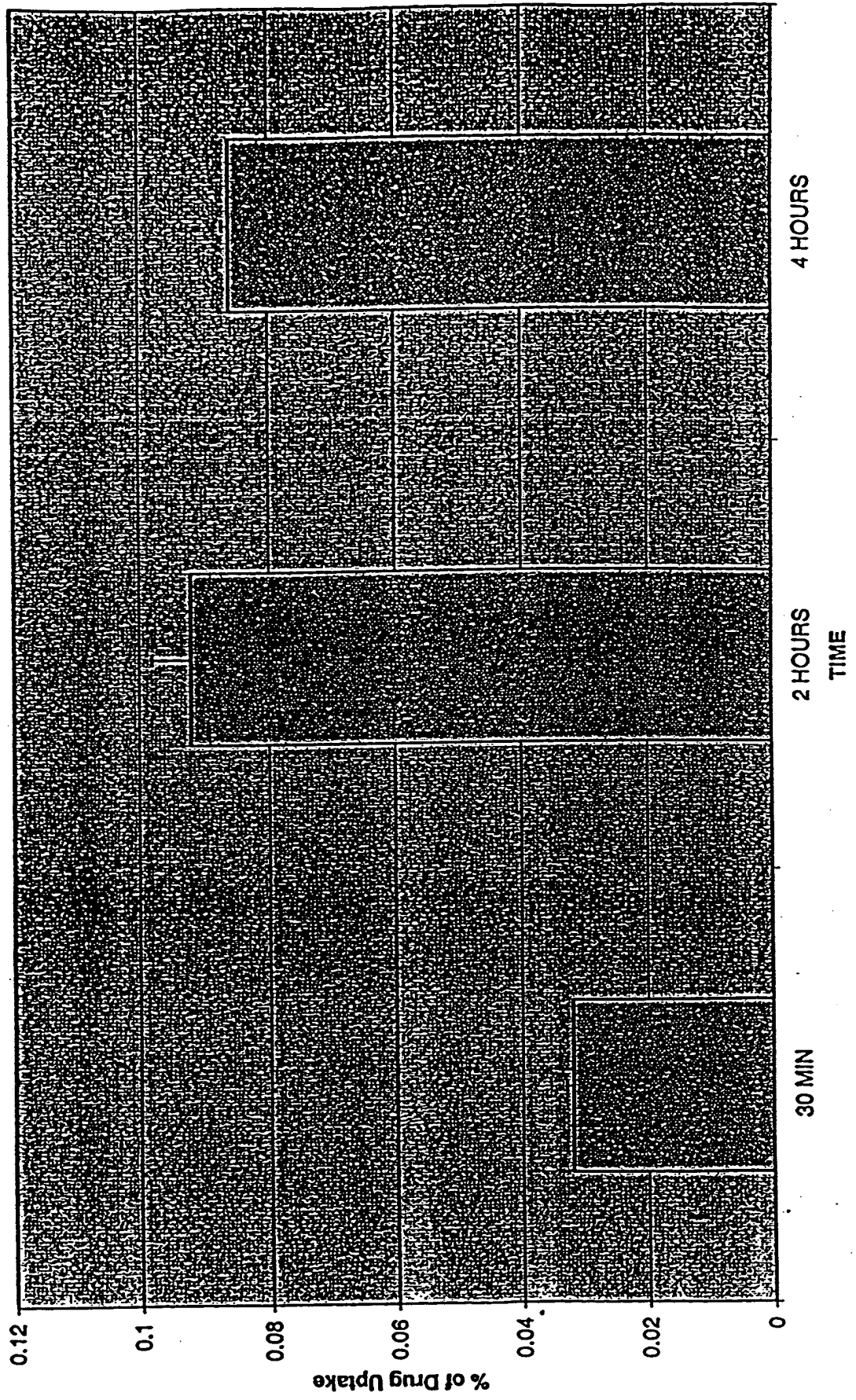


FIG. 55B

In Vitro Cellular Uptake of ^{18}F FDG in Human Lung Cancer Cell Line (A549)

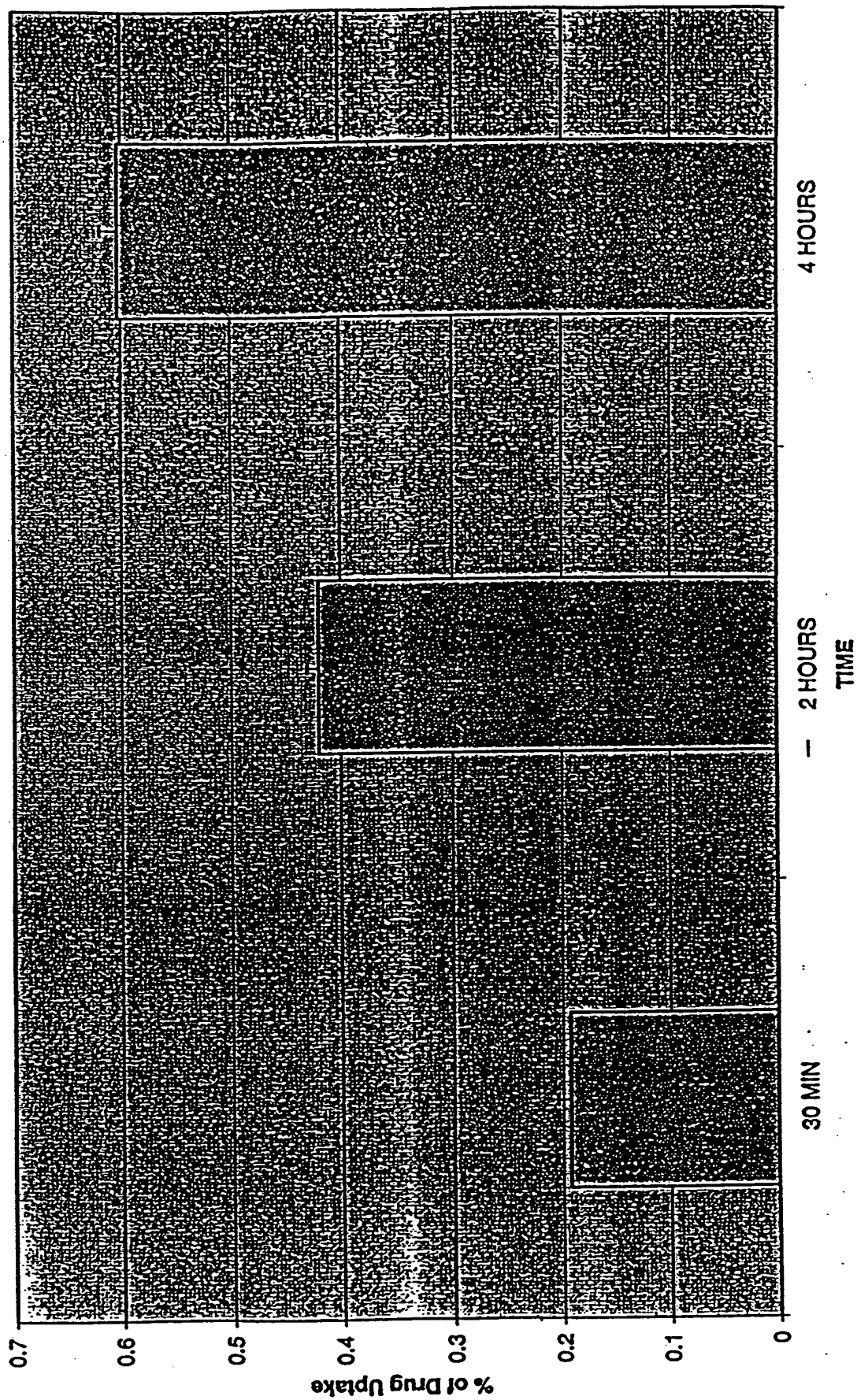


FIG. 55C

Tumor-to-tissue count density ratios of ^{99m}Tc -EC-GAP in breast tumor-bearing rats
(n=3/Interval; 10 μCi /rat, IV)

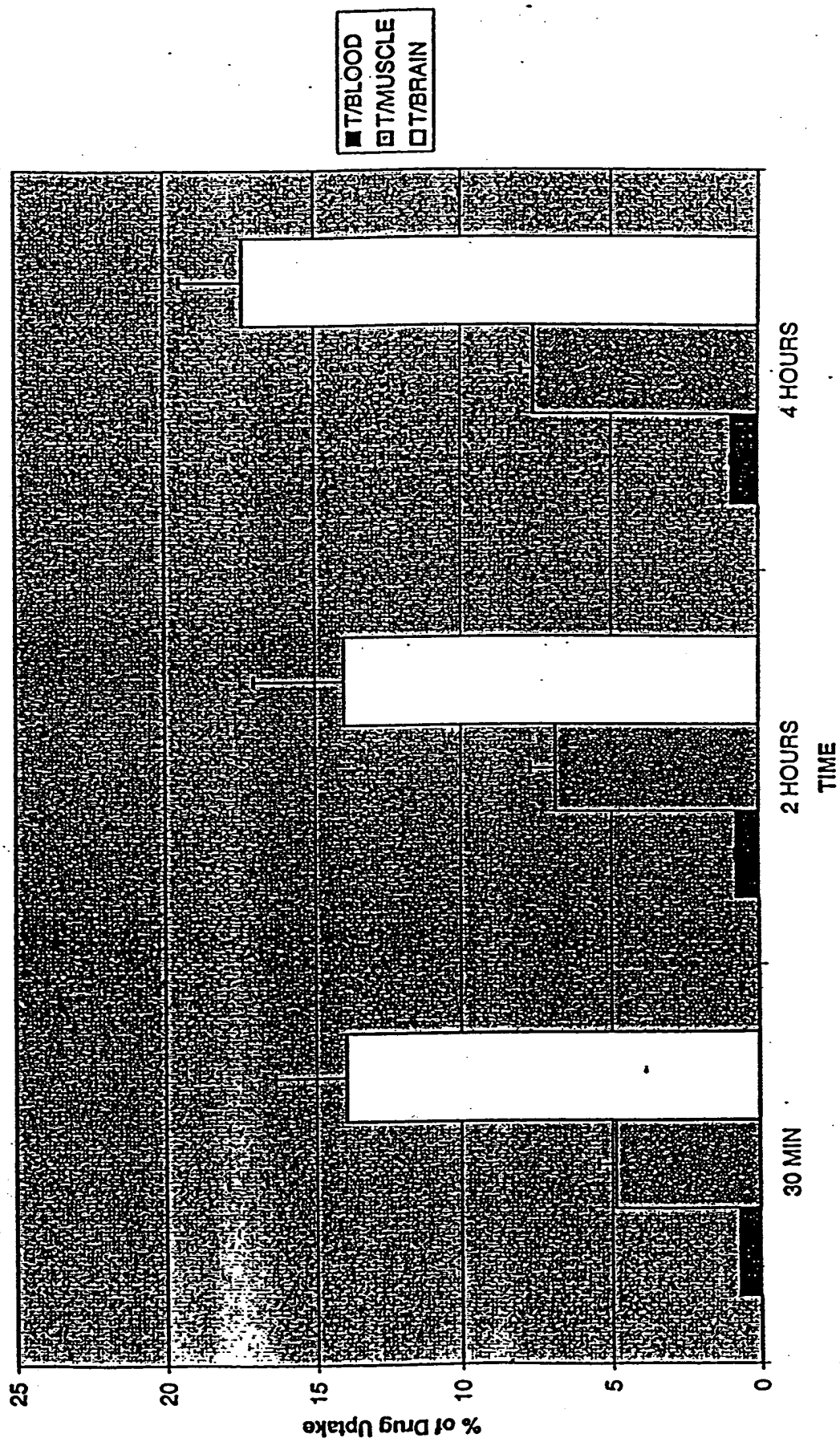


FIG. 56

In Vitro Cellular Uptake of ^{18}F FDG with Glucose Loading at 2 Hours Post-Injection in Breast
Cancer Cell Line (13762)

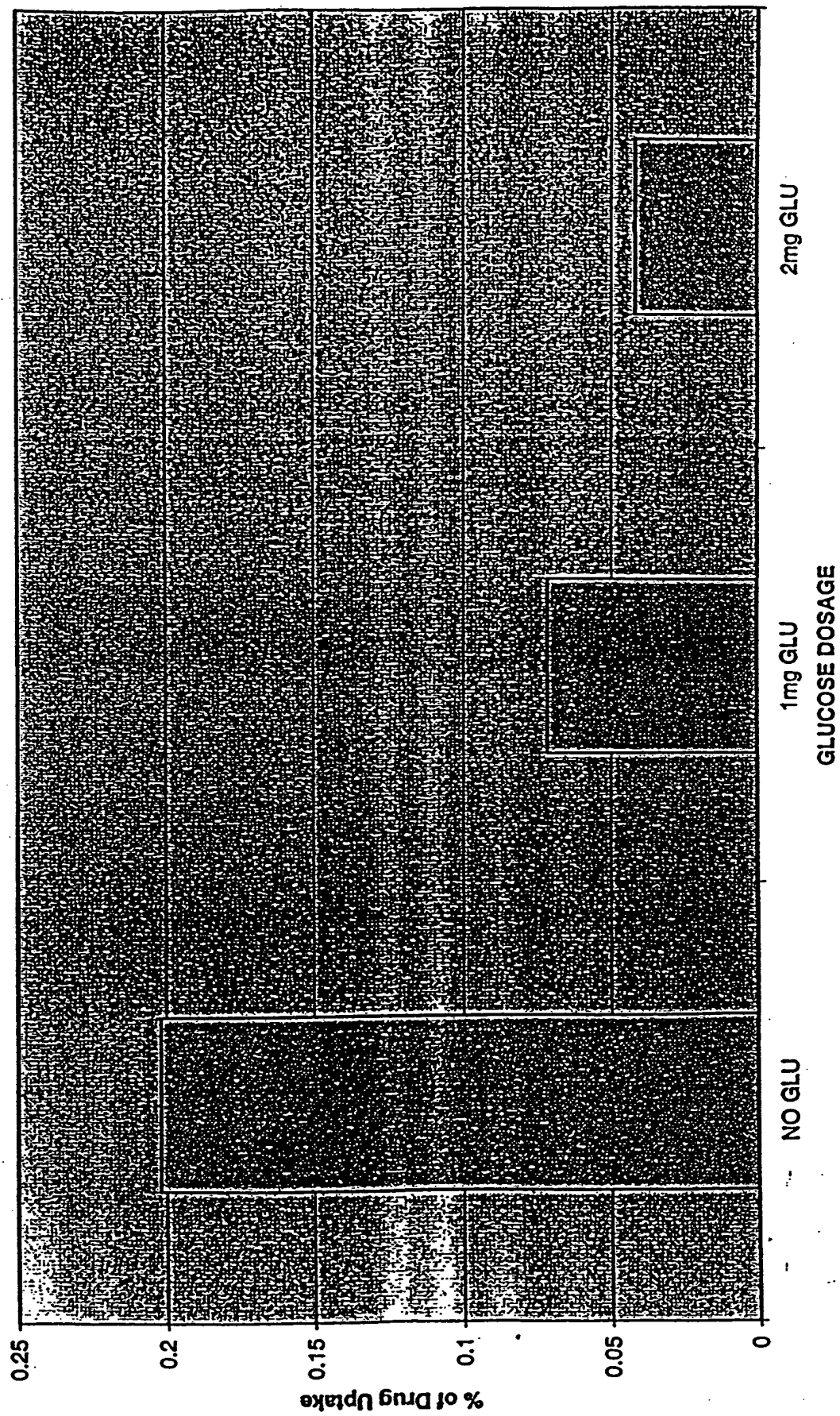


FIG. 57

% Uptake of ^{99m}Tc -EC-Neomycin In Breast Tumor-Bearing Rats

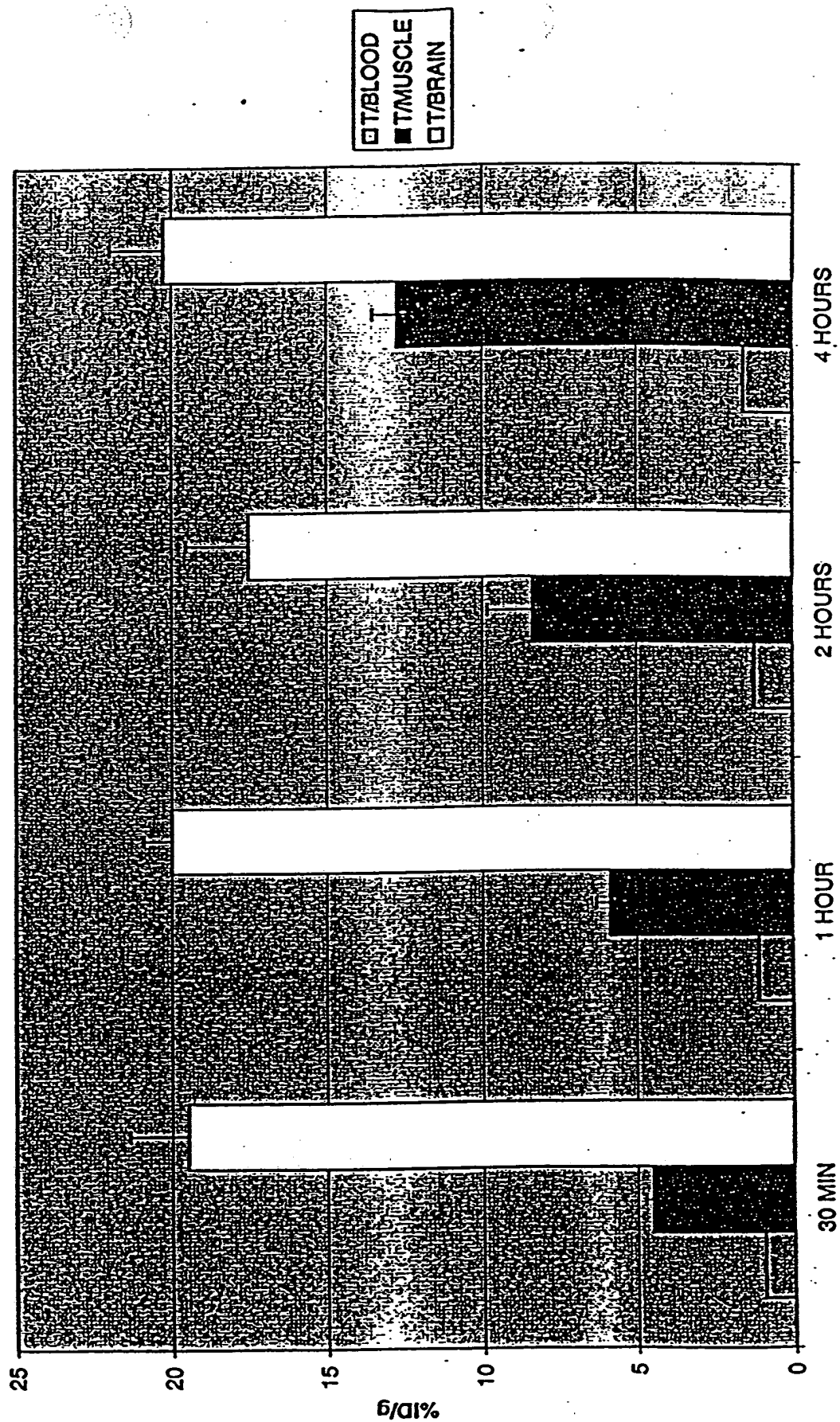
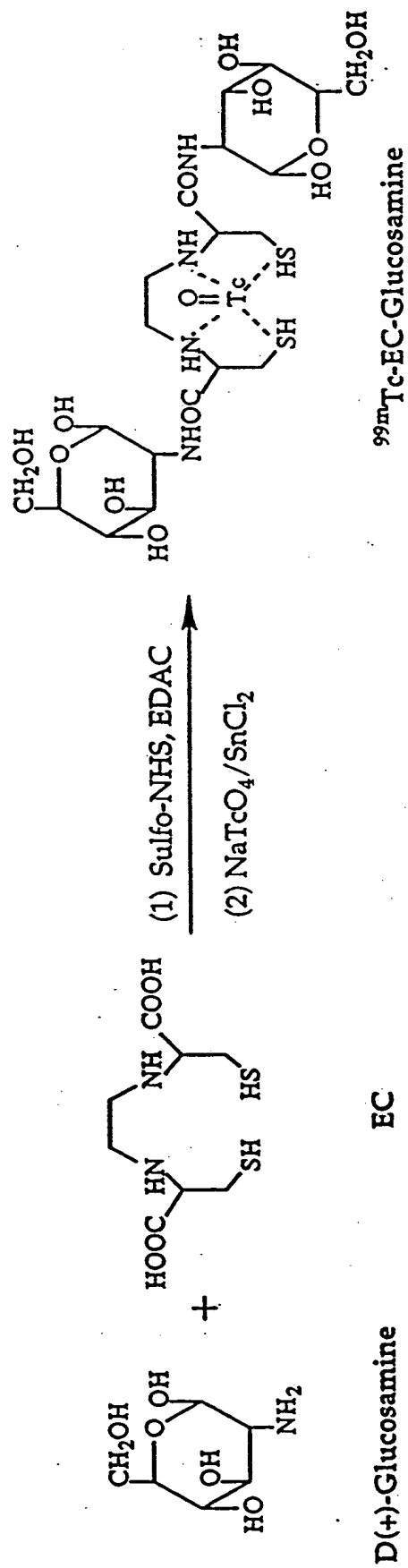


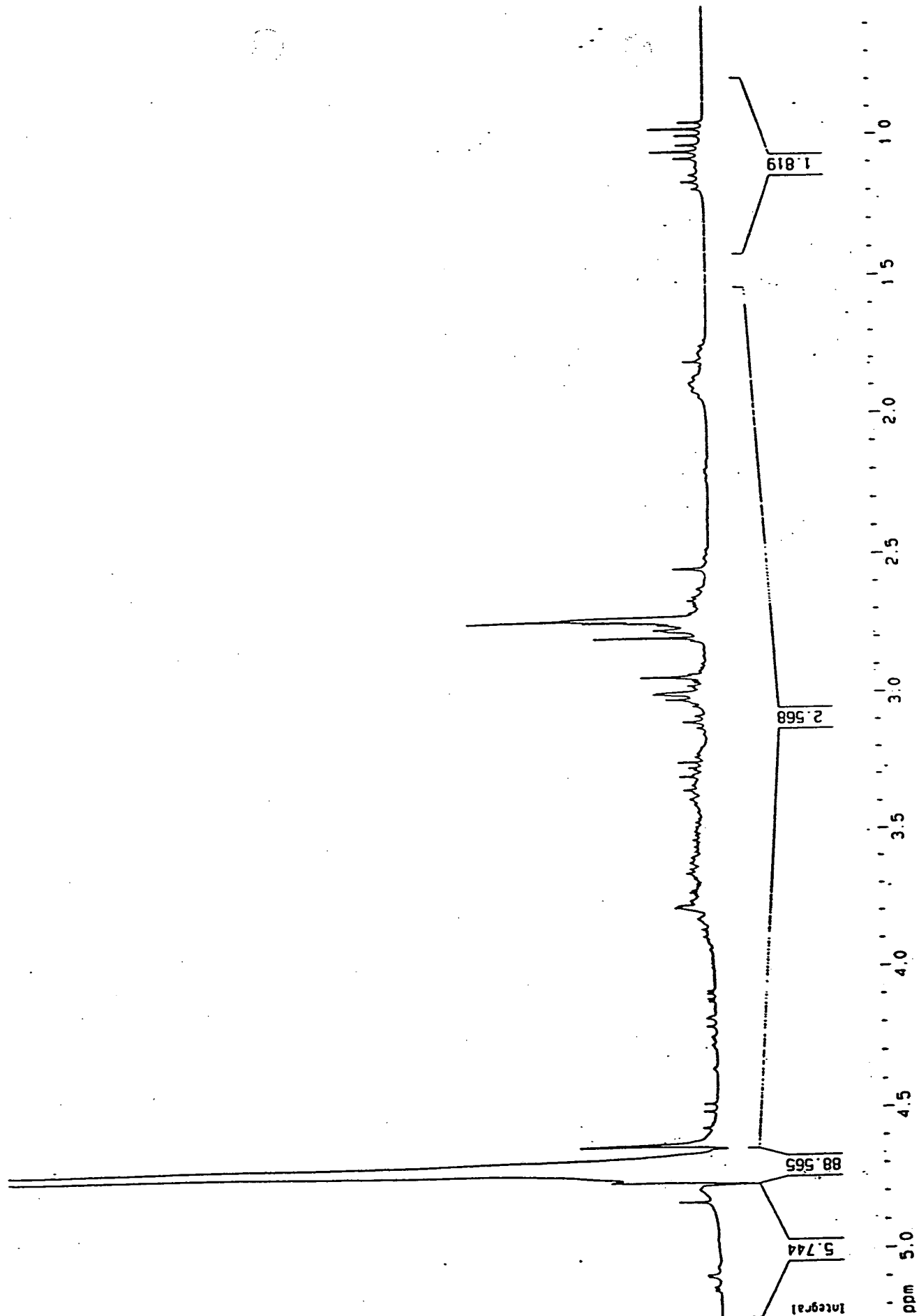
FIG. 58



Synthetic scheme of $^{99\text{m}}\text{Tc-EC-deoxyglucose}$.

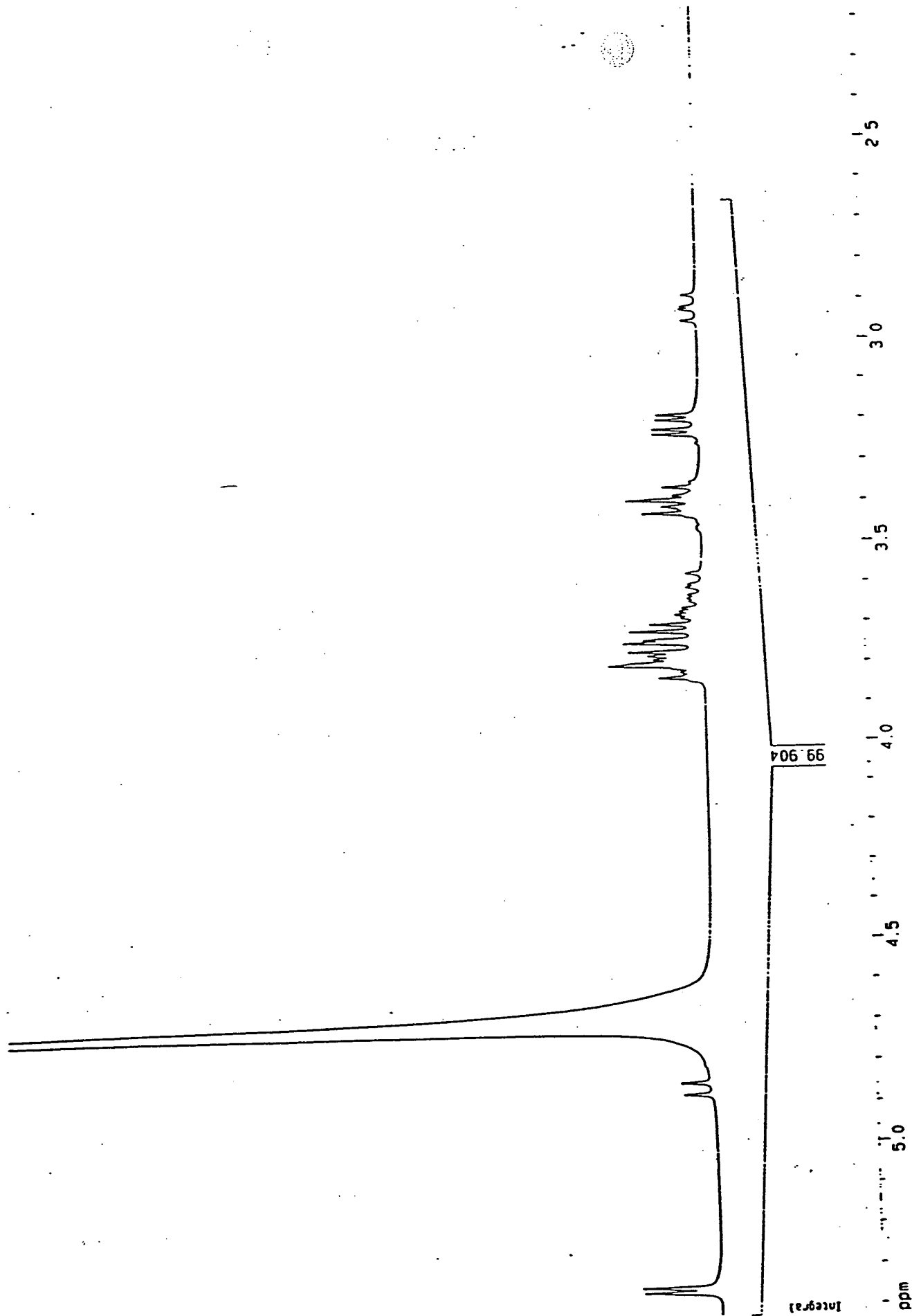
FIG. 59

EC-DG



^1H NMR of EC-deoxyribose (EC-DG).

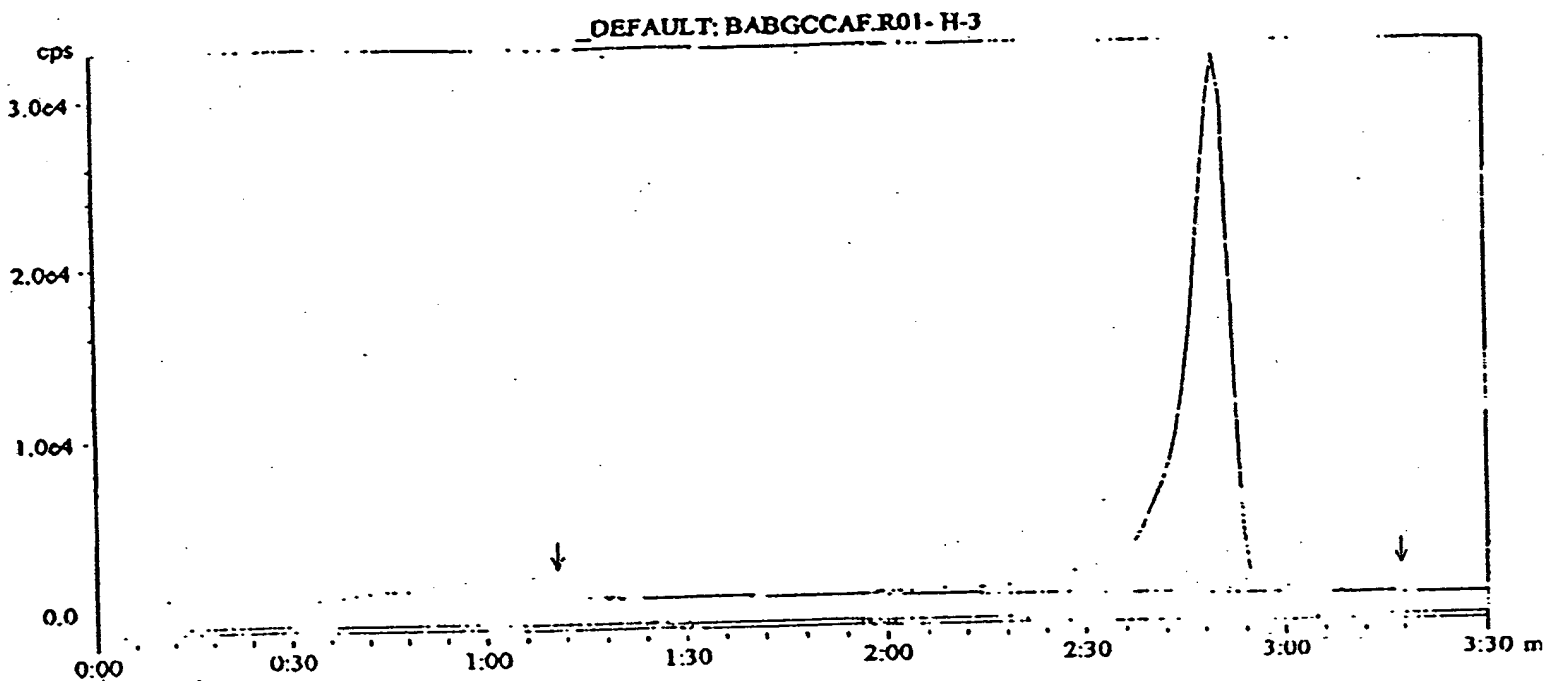
Glucoseamine



^1H -NMR of glucosamine.

04-03 18:55 MON FROM: WON KANG HOSP

Method: DEFAULT File: BABGCCAF.R01 Raw data User: EC-Glucosami

^{99m}Tc-EC-DG TLC

Integrals: BABGCCAF.R01

Channel: H-3	Detector:						
Name	Start - End	RT	Height (cps)	Area (Counts)	%Total (%)	%ROI (%)	
Bkg 1	0:00- 2:19	1:09	539.7				
Rgn 1	2:19- 3:02	2:47	31606.2	263570.8	97.99	100.00	
Bkg 2	3:02- 3:27	3:14	250.1				
1 Peak				263570.8	97.99	100.00	

Total Area = 268986.1 Counts
 Bkg Area = 89999.9 Counts
 Unallocated = 5415.3 Counts (2.01%)

Trace Parameters: BABGCCAF.R01-H-3

Trace Display Smoothing: 0.0 s
 Trace Display Shift: 0.0 s
 Trace Display Factor: 1.000
 Channel Shift: 0.0 s
 Channel Factor: 1.000

Regions were added manually.

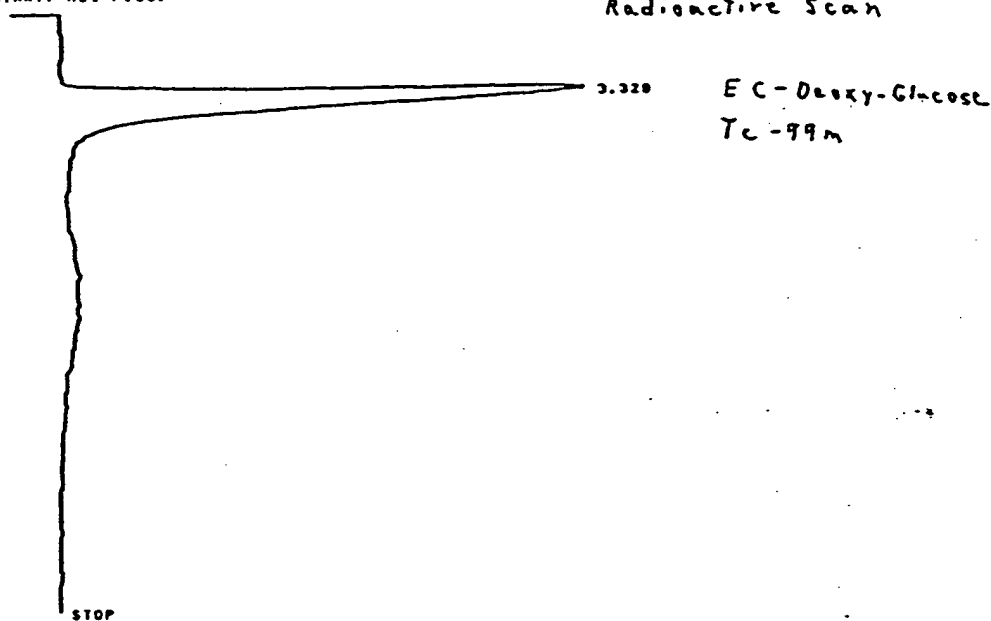
FIG. 63

Radio-TLC analysis of ^{99m}Tc-EC-DG.

^{99m}Tc-EC-deoxyglucose

Rad Aminex HPX-87C
Column
250 x 4 mm
.4 ml/min. H₂O at
85°C
Radioactive Scan

• ATT 2-7 8
• RUN 5 MAR 30, 1999 14143128
START: not ready



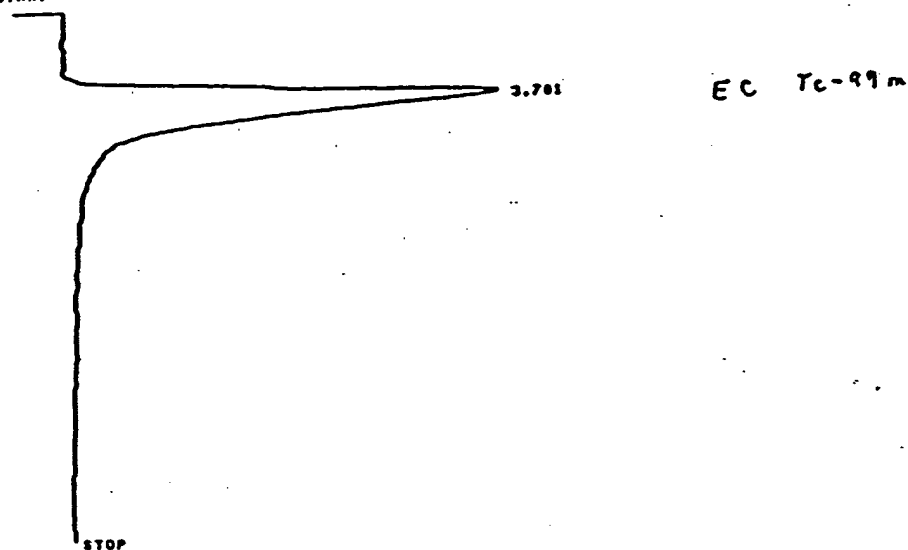
RUN 5 MAR 30, 1999 14143128

RT	AREA	TYPE	WIDTH	AREA
3.320	33350000	SV	.813	100.00000

TOTAL AREA=3.3350E+07
NUL FACTOR=1.0000E+00

Radioactive Scan

• RUN 6 MAR 30, 1999 15109139
START



RUN 6 MAR 30, 1999 15109139

RT	AREA	TYPE	WIDTH	AREA
3.701	16673104	SV	.310	100.00000

TOTAL AREA=1.6671E+07

^{99m}Tc-EC

FIG. 64

HPLC analysis of ^{99m}Tc-EC-deoxyglucose and ^{99m}Tc-EC-
(radioactive detector).

• ATT 2^ BREAK

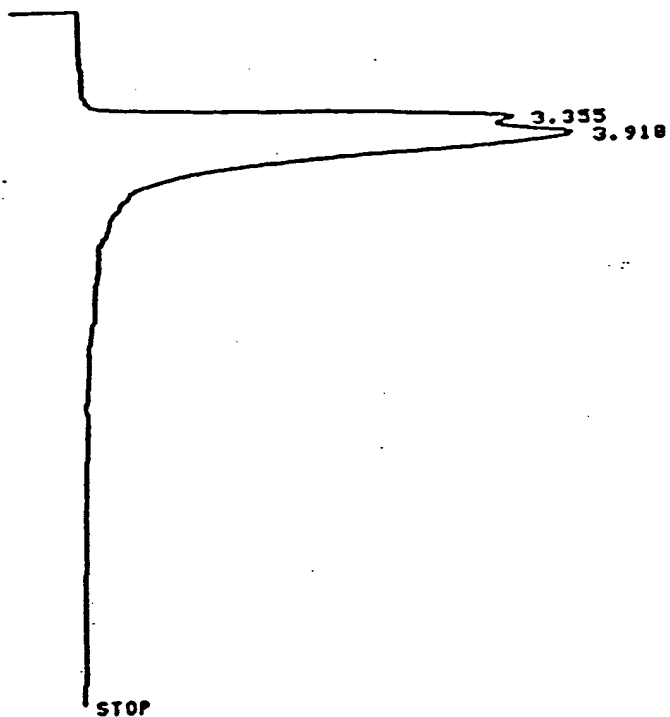
BREAK

• LIST: ATT 2^ = 7

• ATT 2^ 8 0

• RUN 0 7 MAR 30, 1999 15132137

START



Radioactive Scan

Mixed Tc-99m
EC-Deoxy-Glucose
EC

^{99m}Tc-EC-deoxyglucose + ^{99m}Tc-EC
(mixed)

RUN 0 7 MAR 30, 1999 15132137

AREA	RT	AREA	TYPE	WIDTH	AREA%
	3.355	22173760	BV	.448	50.46186
	3.918	21767872	VV	.387	49.53814

TOTAL AREA=4.3942E+07
MUL FACTOR=1.0000E+00

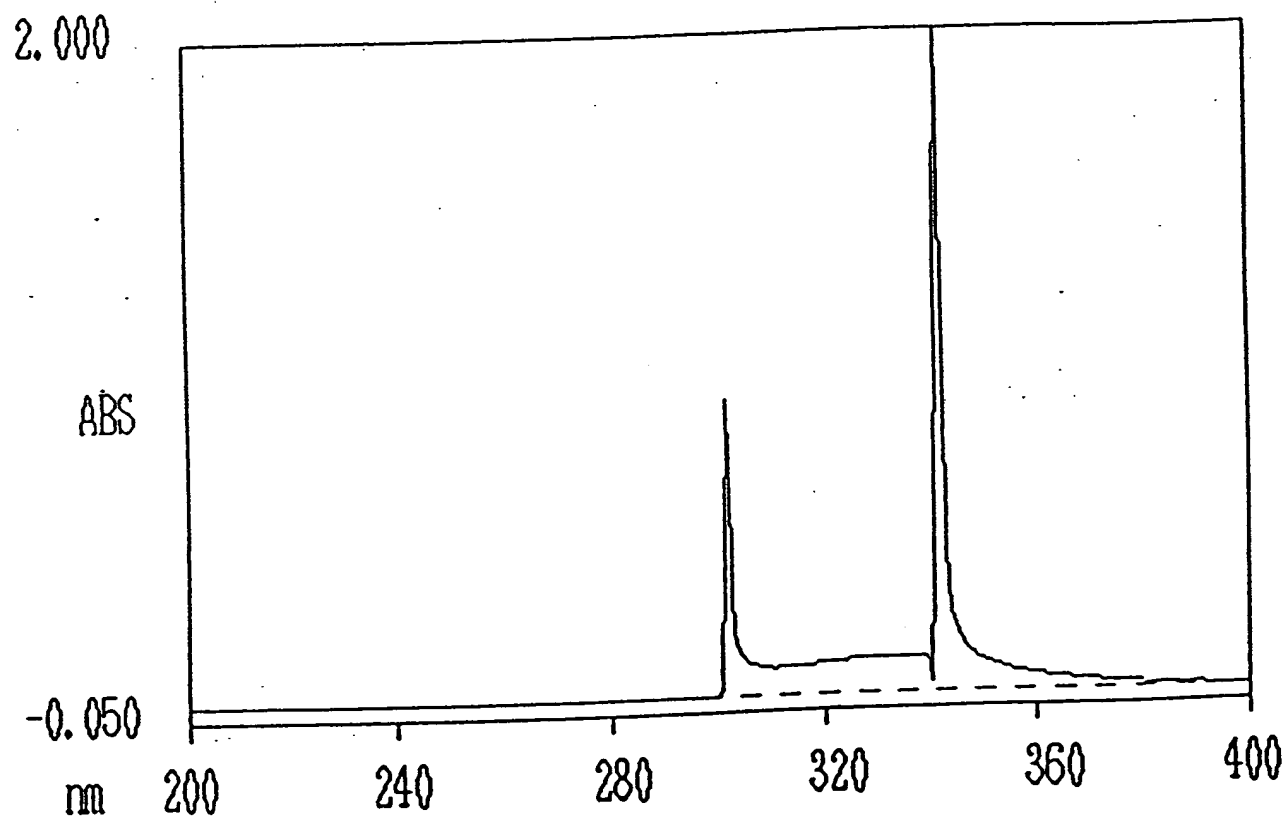
FIG. 65

HPLC analysis of ^{99m}Tc-EC-deoxyglucose and ^{99m}Tc-EC
(radioactive detector, mixed).

Hexokinase Assay of Glucose

WAVELENGTH SCAN/0

03/01/00 14:41



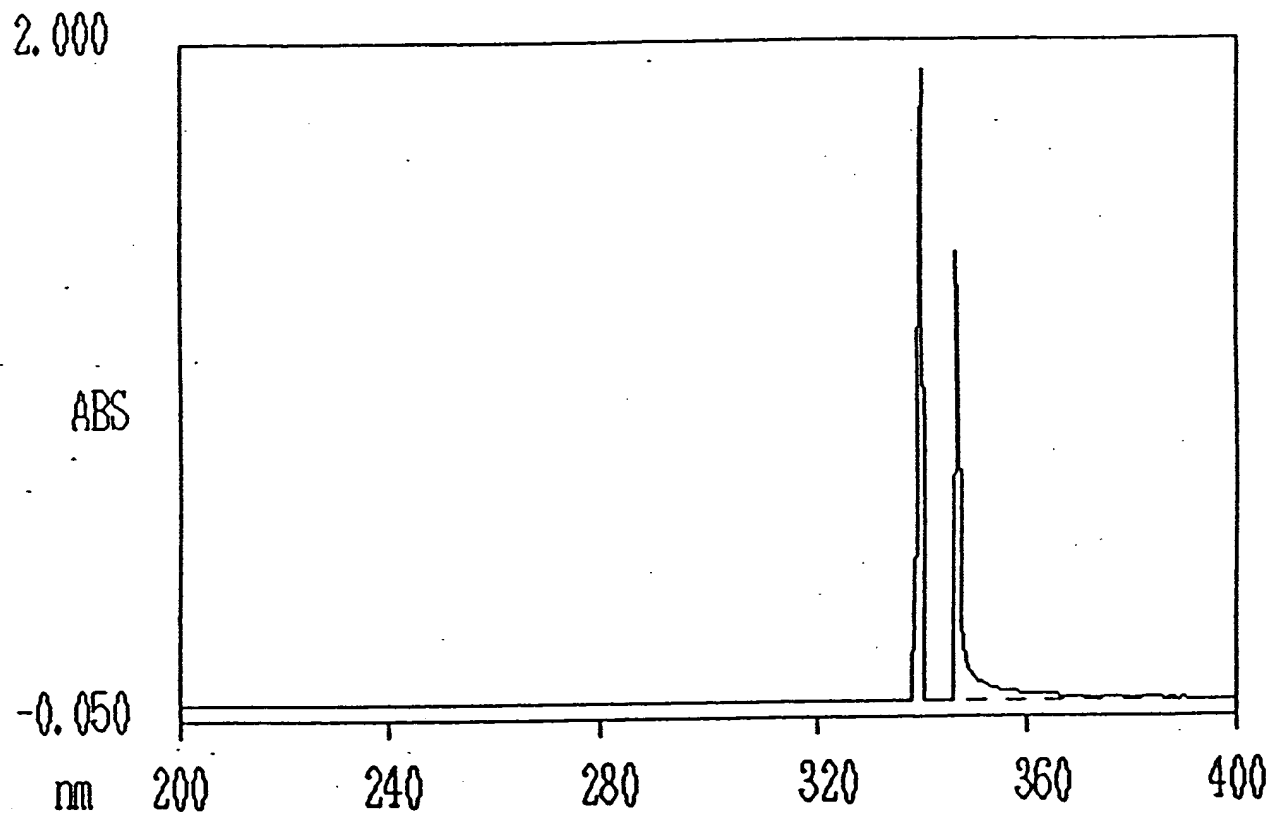
301.5 nm 0.889 ABS
342.0 nm 2.044 ABS

FIG. 66 Hexokinase assay of glucose.

Hexokinase Assay of FDG

WAVELENGTH SCAN/0

03/09/00 14:34



340.0 nm 1.906 ABS
346.5 nm 1.351 ABS

FIG. 67

Hexokinase assay of FDG.

Hexokinase Assay of EC-Glucosamine (EC-DG)

WAVELENGTH SCAN/0

03/01/00 14:45

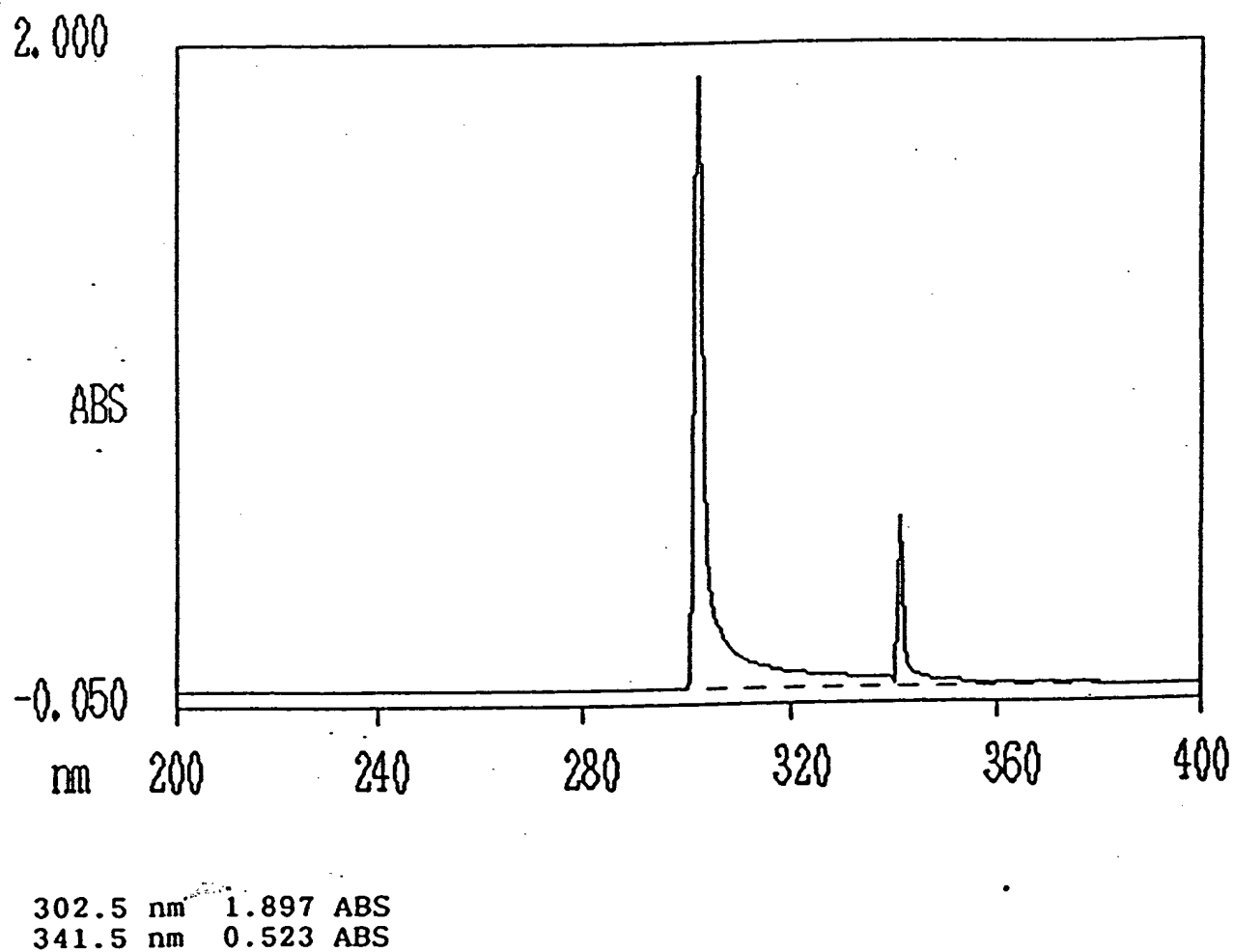


FIG. 68

Hexokinase assay of EC-DG.

% of Drug Uptake In Lung Cancer Cell Line (A549)

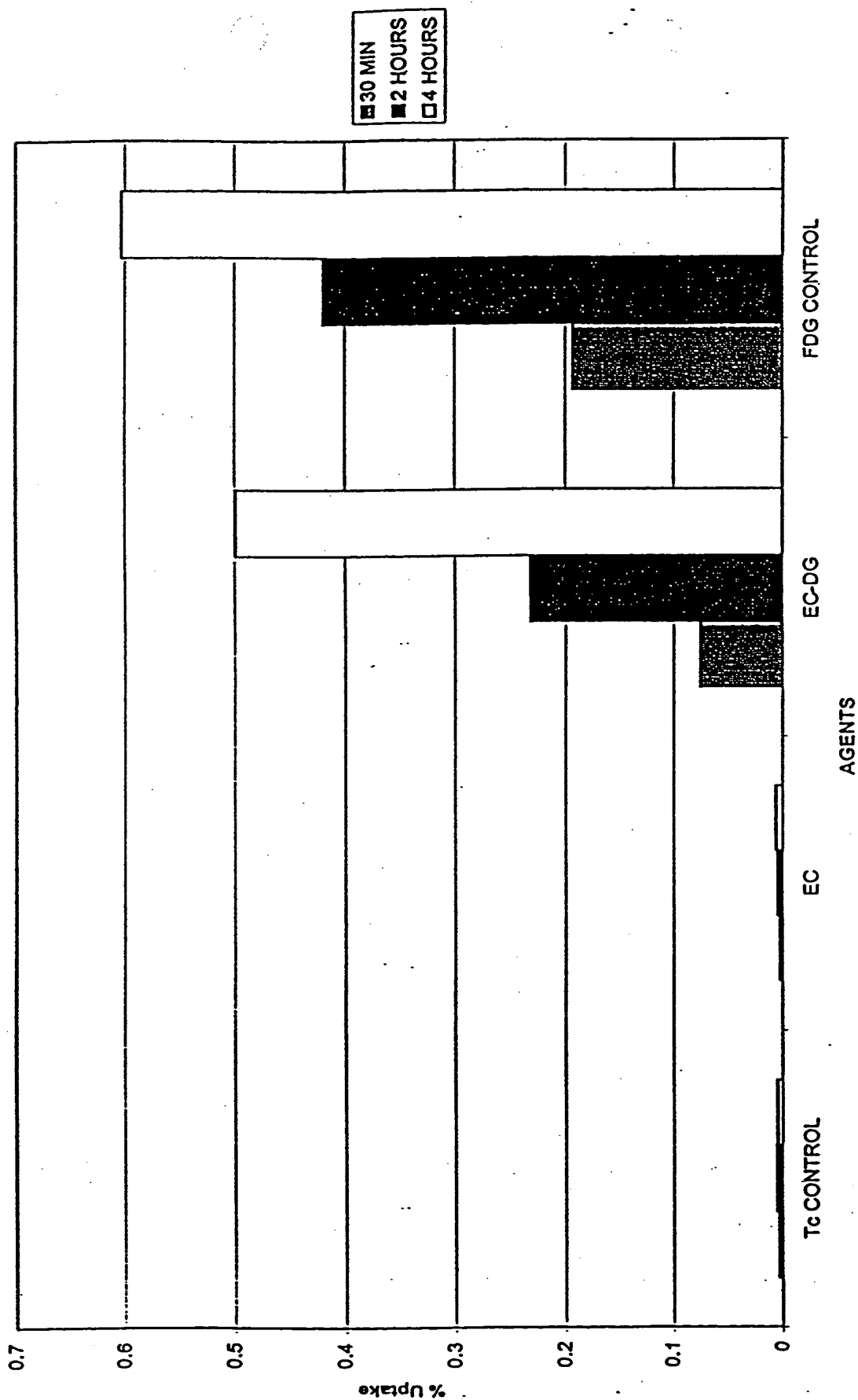


FIG. 69 In vitro cellular uptake assay of ^{99m}Tc -EC-deoxyglucose, ^{99m}Tc -EC and ^{18}F -FDG in lung cancer cell line (A549). ^{99m}Tc -EC-DG showed similar uptake compared to ^{18}F -FDG.

***In Vitro* Cellular Uptake of ^{99m}Tc -EC-DG in Breast Cancer Cells after Glucose Loading (2 hours
incubation; 2uCi/well; 50,000 cells/well; 0.5mL/well)**

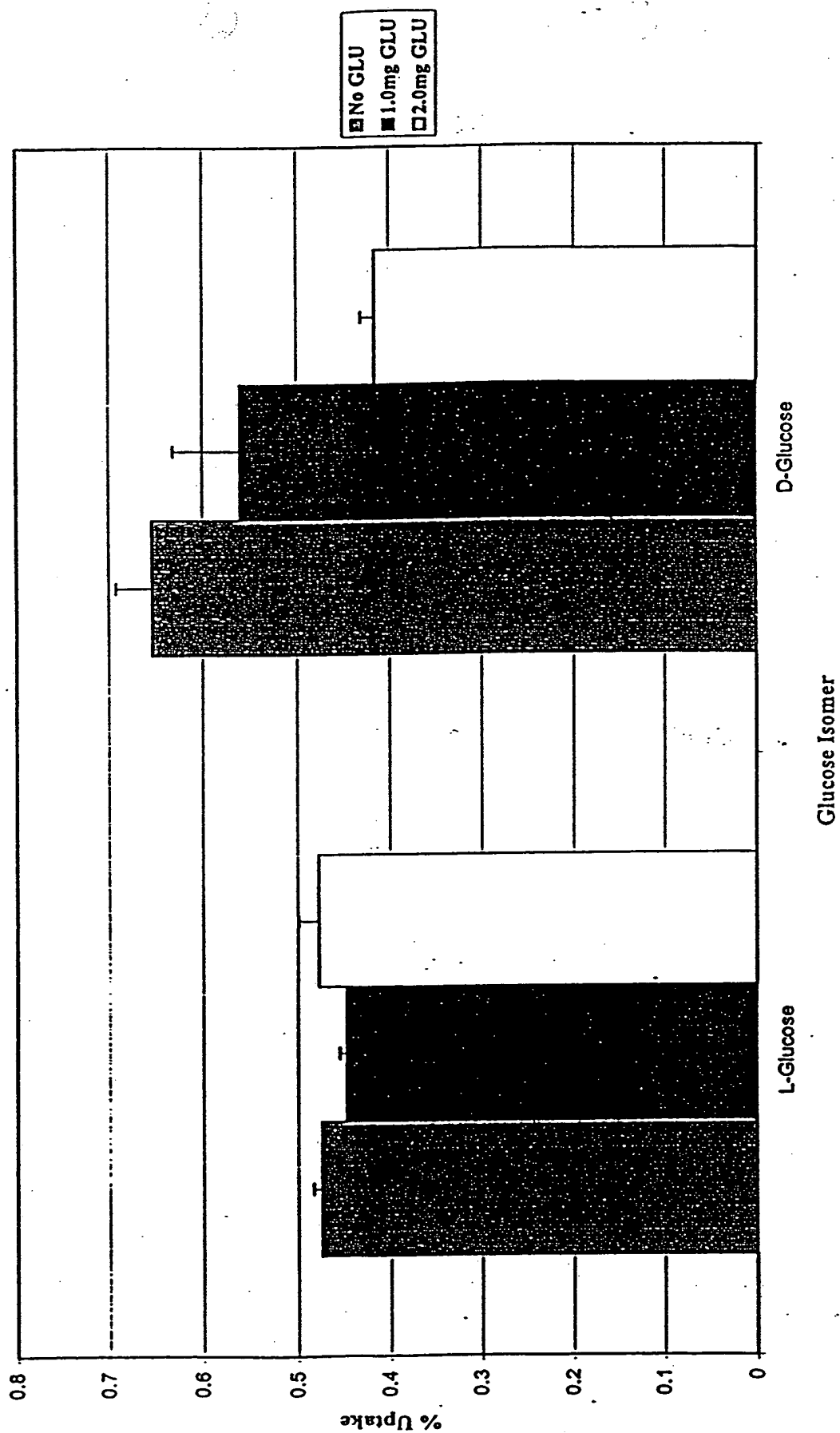


FIG. 70
Effect of d- and l-glucose on breast cellular (13762 cell line) uptake
of ^{99m}Tc -EC-DG.

In Vitro Cellular Uptake of ^{18}F FDG in Breast Cancer Cells after Glucose Loading (2 hours
Incubation; 2uCi/well; 50,000 cells/well; 5mL/well)

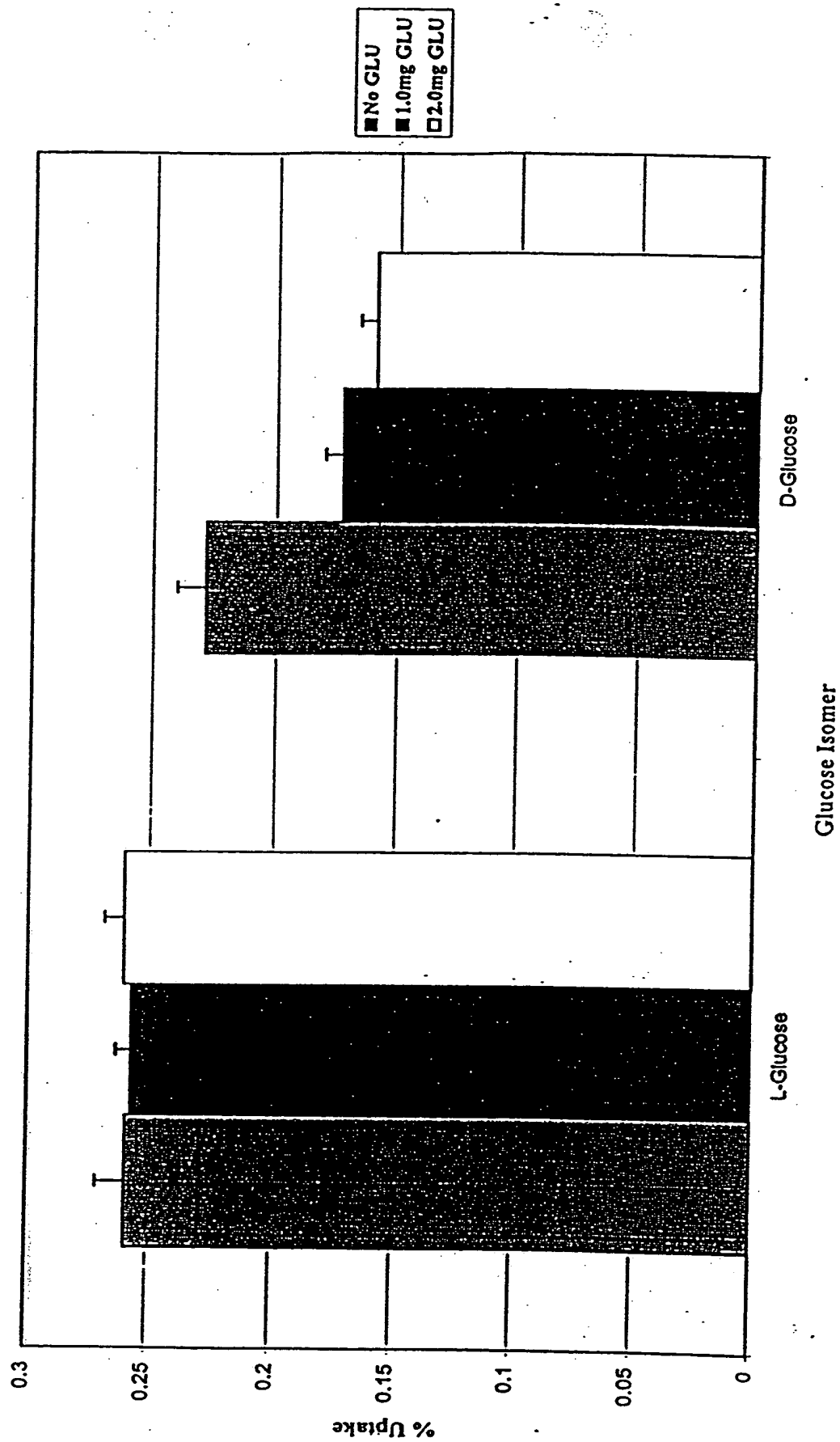


FIG. 71 Effect of d- and l-glucose on breast cellular (13762 cell line) uptake of ^{18}F -FDG.

***In Vitro* Cellular Uptake of ^{18}F FDG in Lung Cancer Cells after Glucose Loading (2 hours incubation;
2uCi/well; 50,000 cells/well; 5mL/well)**

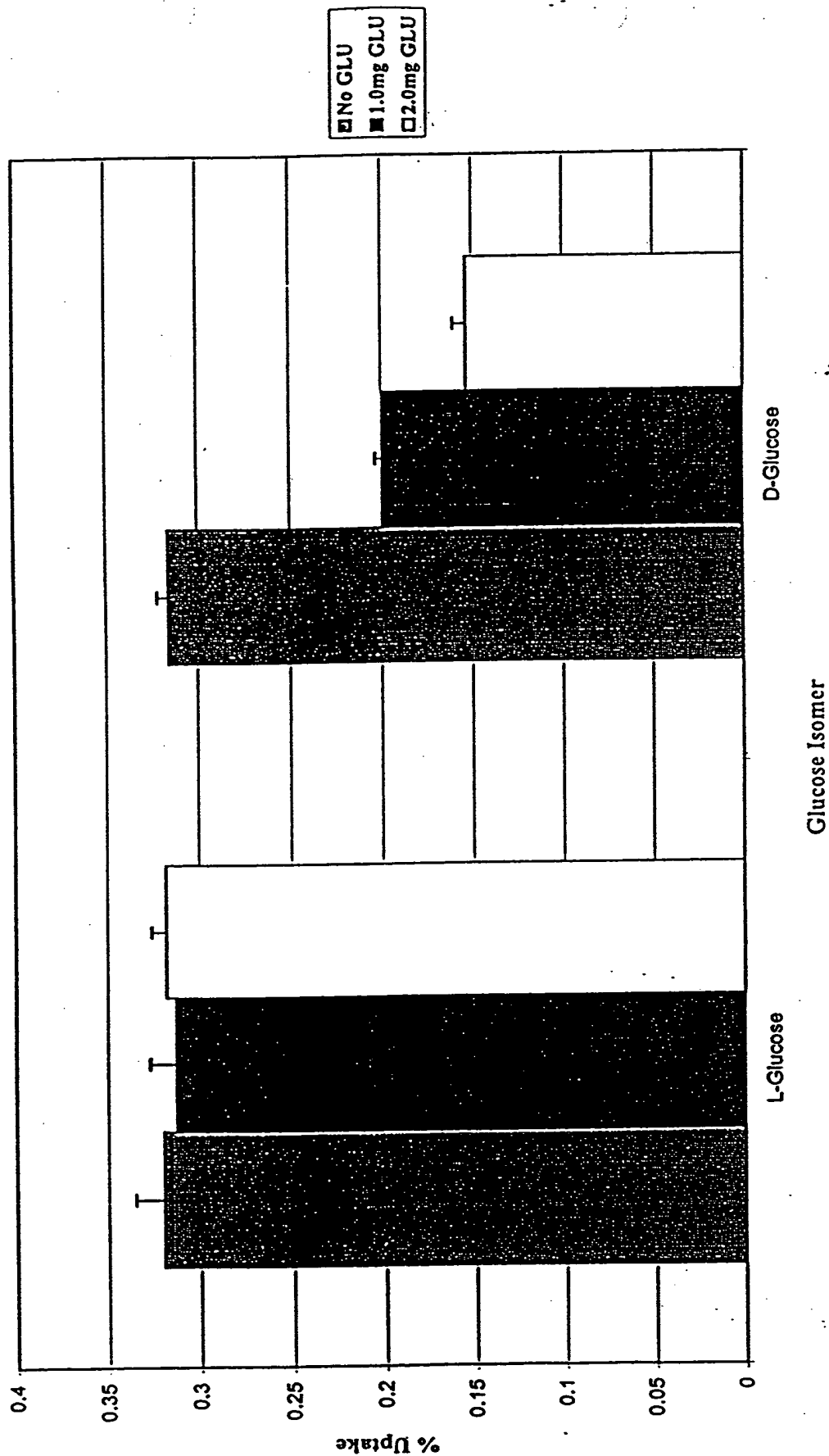


FIG. 72 Effect of d- and l-glucose on lungcellular (A549 cell line) uptake of ^{18}F -FDG.

***In Vitro* Cellular Uptake of ^{99m}Tc -EC-DG in Lung Cancer Cells after Glucose Loading (2 hours incubation; 2uCi/well; 50,000 cells/well; 0.5mL/well)**

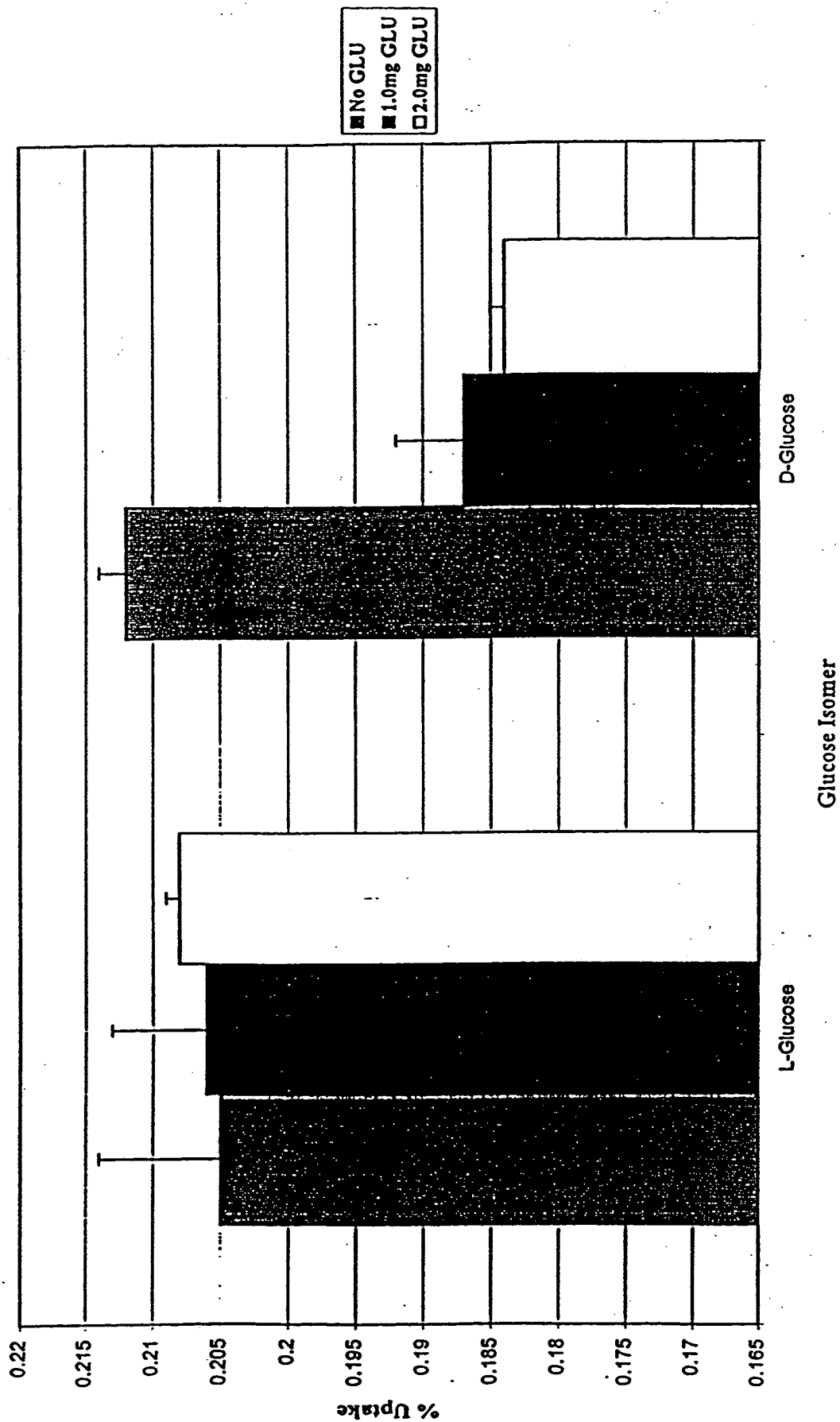


FIG. 73 Effect of d- and l-glucose on breast cellular (A549 cell line) uptake of ^{99m}Tc -EC-DG.

Effect of Intravenous Injection of Glucosamine and EC-DG on Blood Glucose Level in Rats

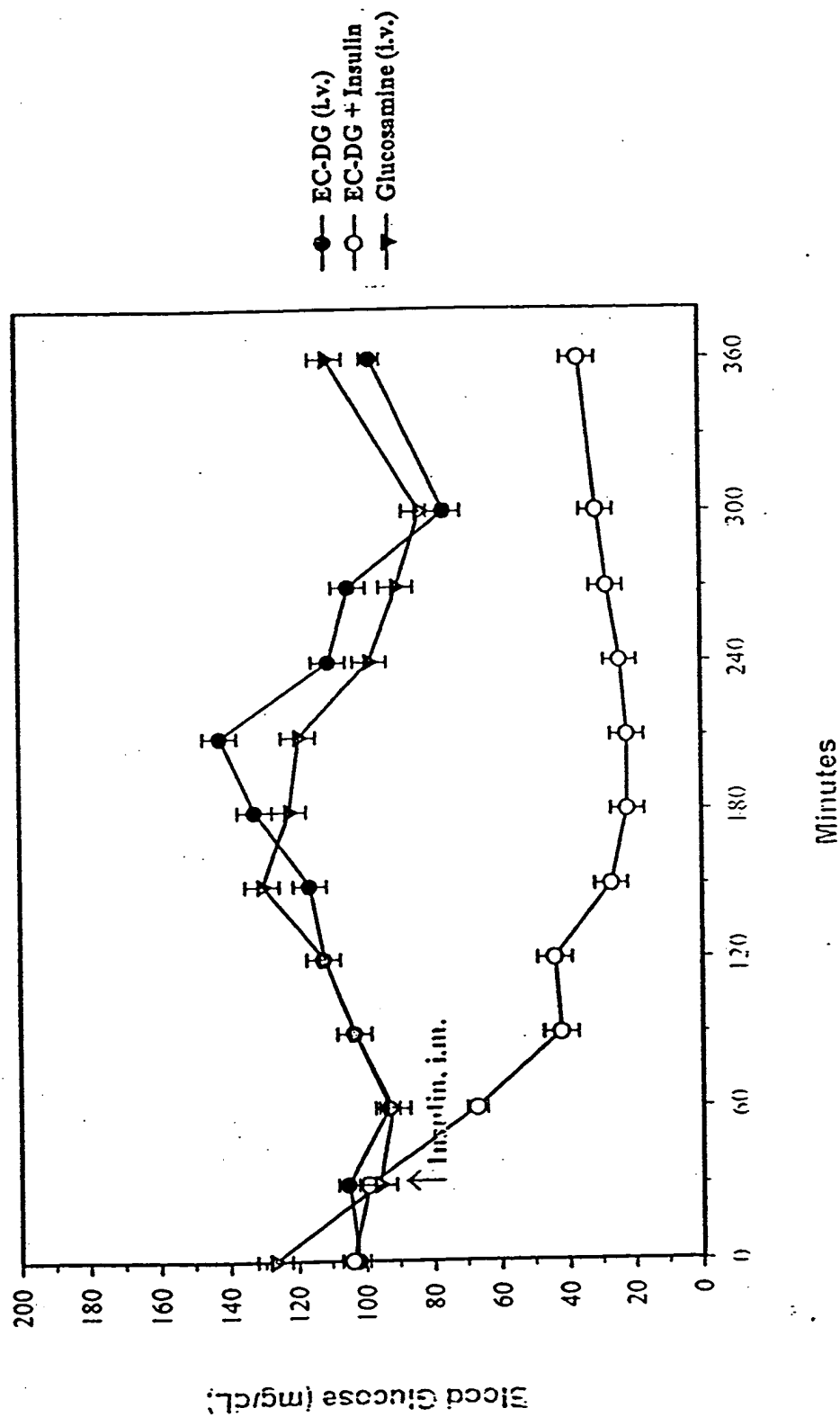


FIG. 74
Effect of *in vivo* blood glucose level induced by glucosamine and EC-DG (1.2 mmol/kg, i.v.).

Effect of Intravenous Injection of FDG and FDG+Insulin on Blood Glucose Level in Rats

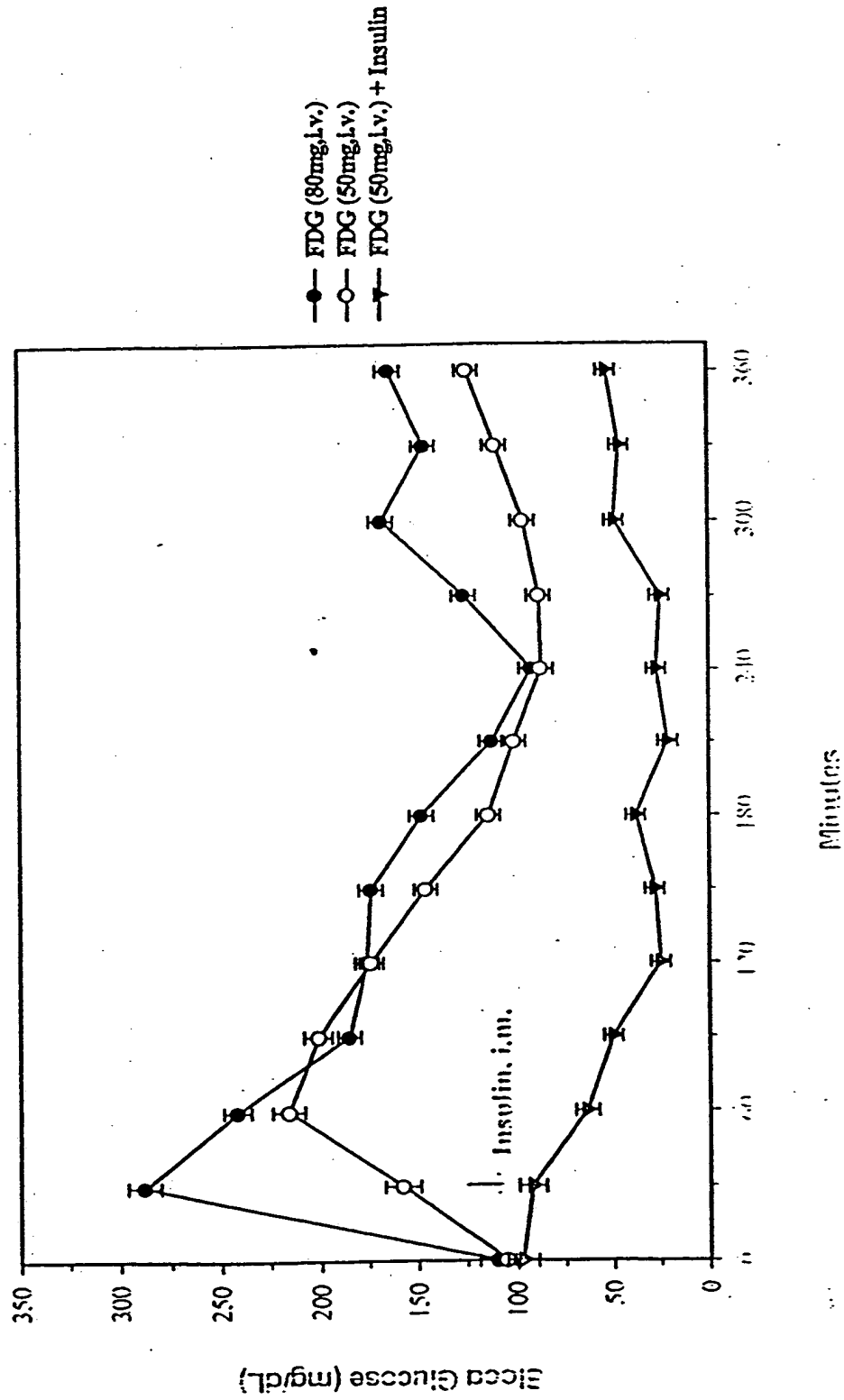


FIG. 75 Effect of *in vivo* blood glucose level induced by FDG (1.2 and 1.9 mmol/kg, i.v.) and insulin.

Tumor-to-Tissue Count Density Ratios of ^{99m}Tc -EC-Deoxyglucose in Breast Tumor-Bearing Rats

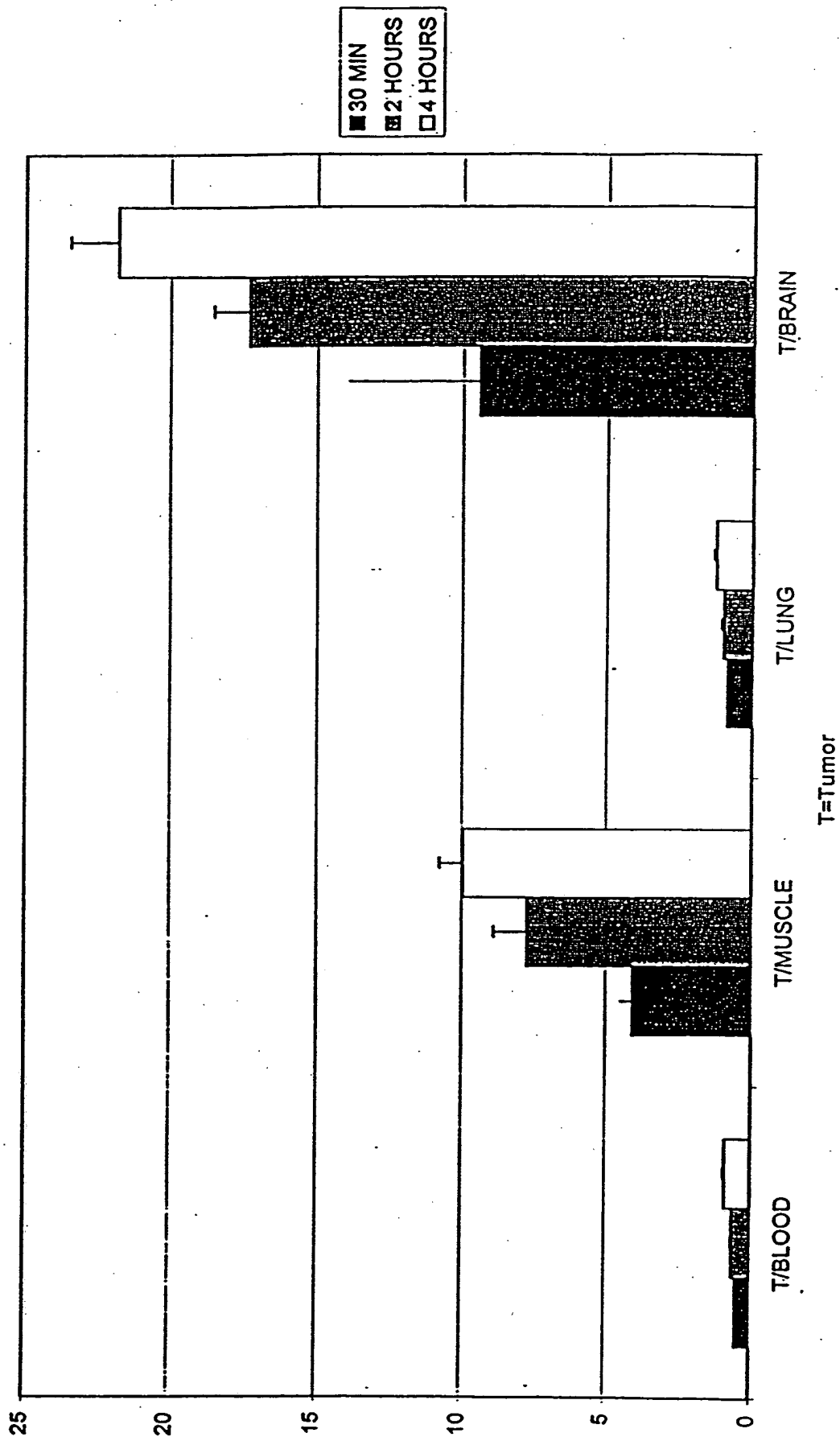


FIG. 76 Tumor-to-tissue count density ratios of ^{99m}Tc -EC-deoxyglucose in breast tumor-bearing rats.

In Vivo Uptake of ^{99m}Tc -EC-Deoxyglucose in Breast Tumor-Bearing Rats

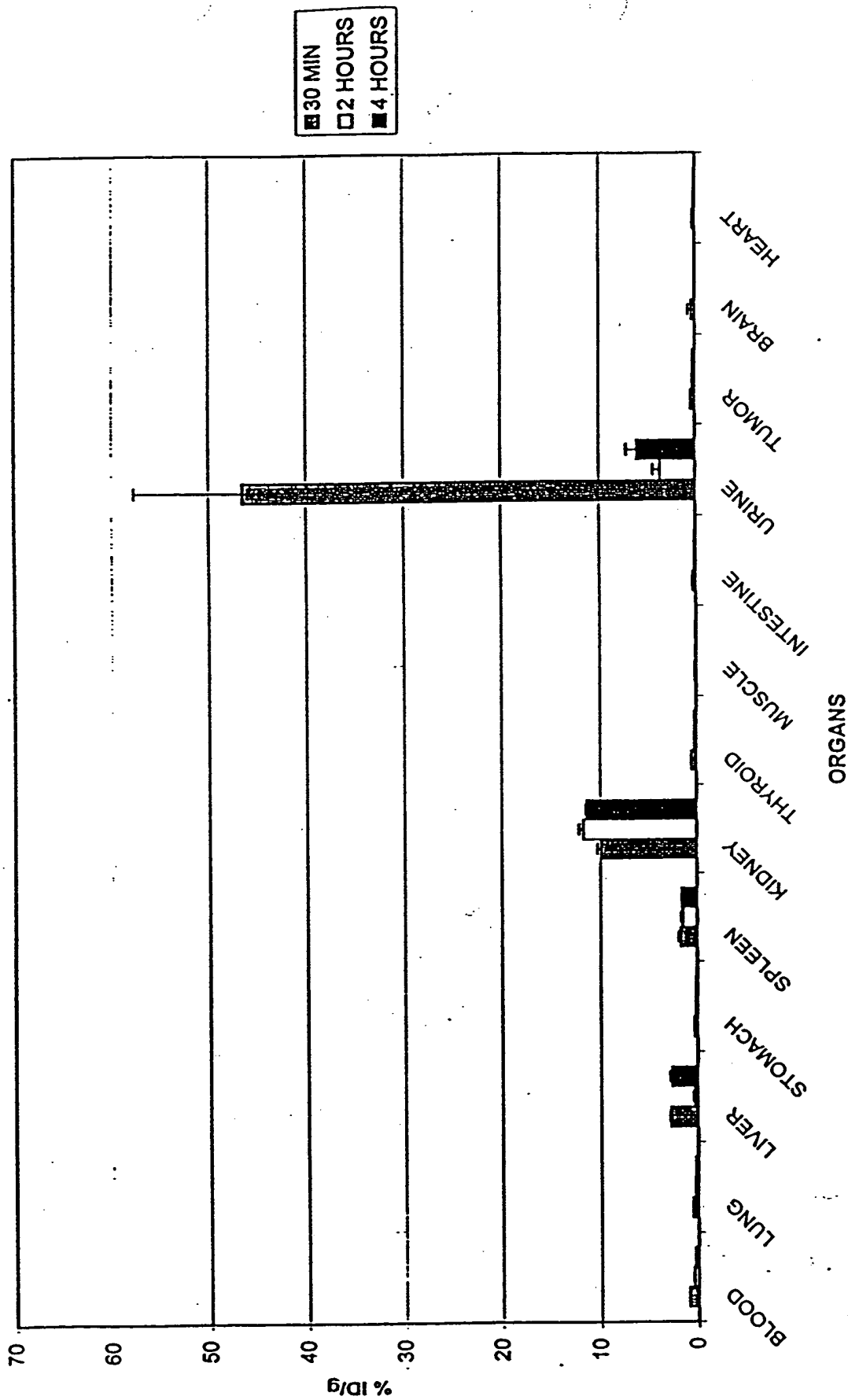


FIG. 77 In vivo biodistribution of ^{99m}Tc -EC-deoxyglucose in breast tumor-bearing rats.

In Vivo Uptake of ^{99m}Tc -EC-Deoxyglucose in Lung Tumor-Bearing Nude Mice

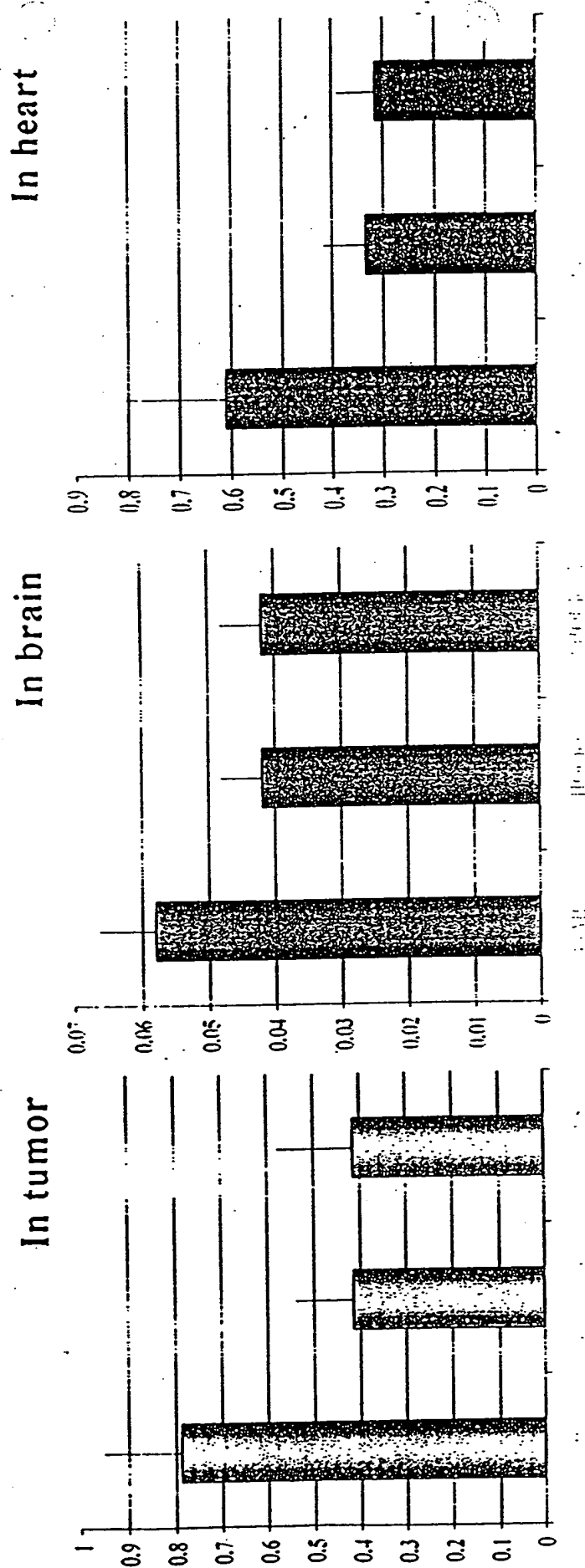


FIG. 78 In vivo tissue uptake of ^{99m}Tc -EC-deoxyglucose in lung tumor-bearing mice.

In Vivo Uptake of ^{99m}Tc -EC-Neomycin in Lung Tumor-Bearing Nude Mice

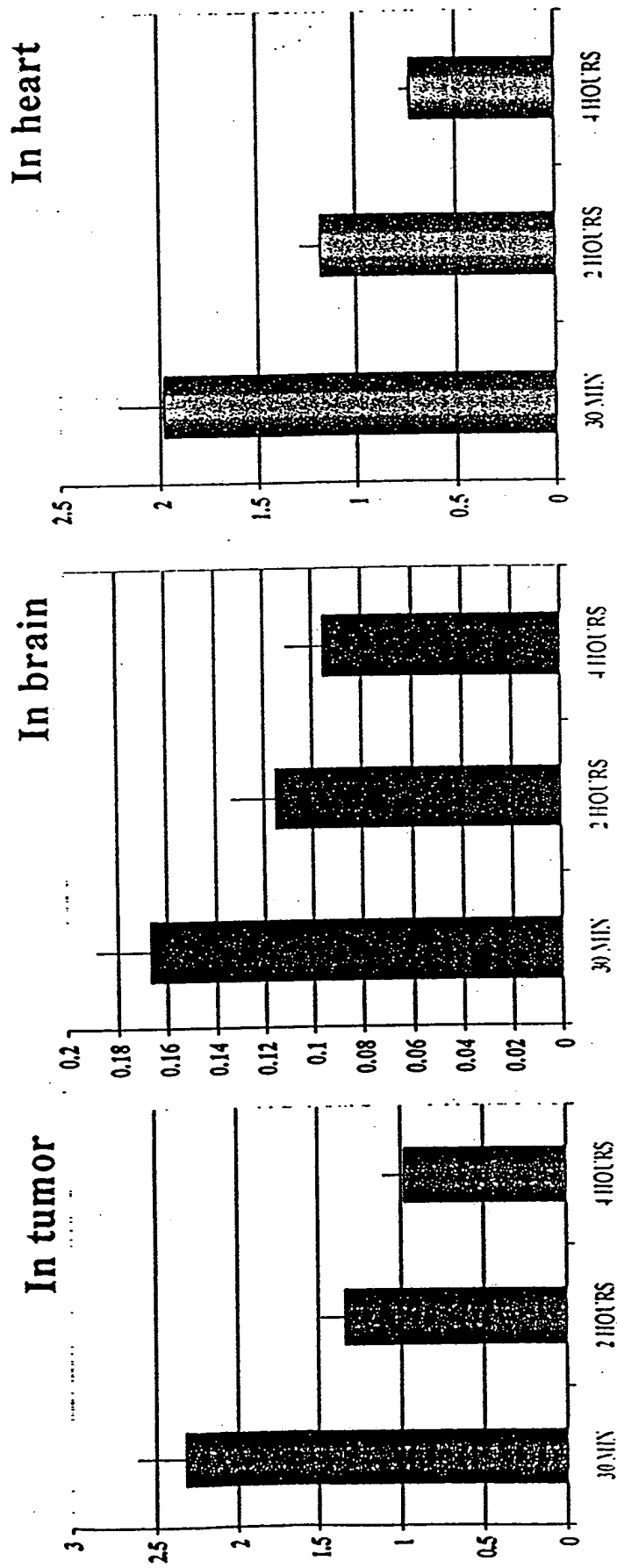


FIG. 79 In vivo tissue uptake of ^{99m}Tc -EC-neomycin in lung tumor-bearing mice.

In Vivo Uptake of ^{18}F FDG in Lung Tumor-Bearing Nude Mice

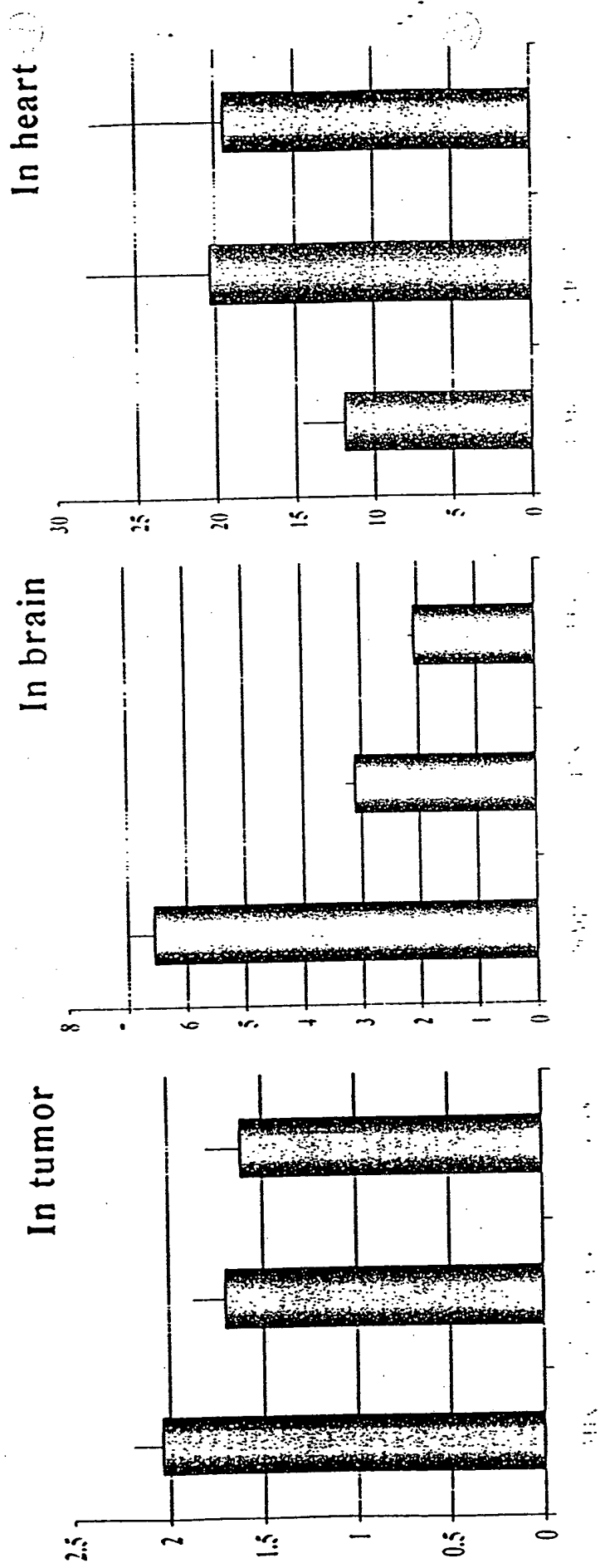
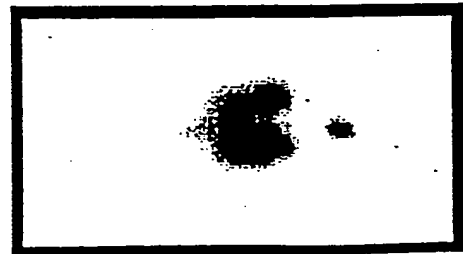


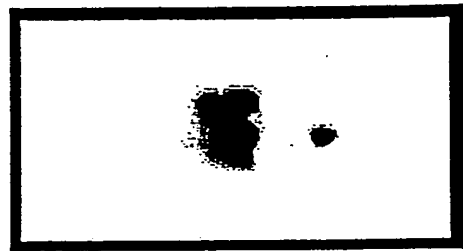
FIG. 80 In vivo tissue uptake of ^{18}F -FDG in lung tumor-bearing mice.

$^{99m}\text{Tc-EC}$

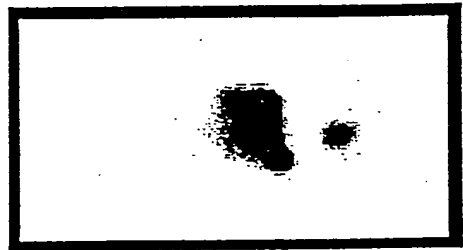
$^{99m}\text{Tc-EC-Glucose(6)}$



0.5



2



4hrs



0.5



2



4hrs

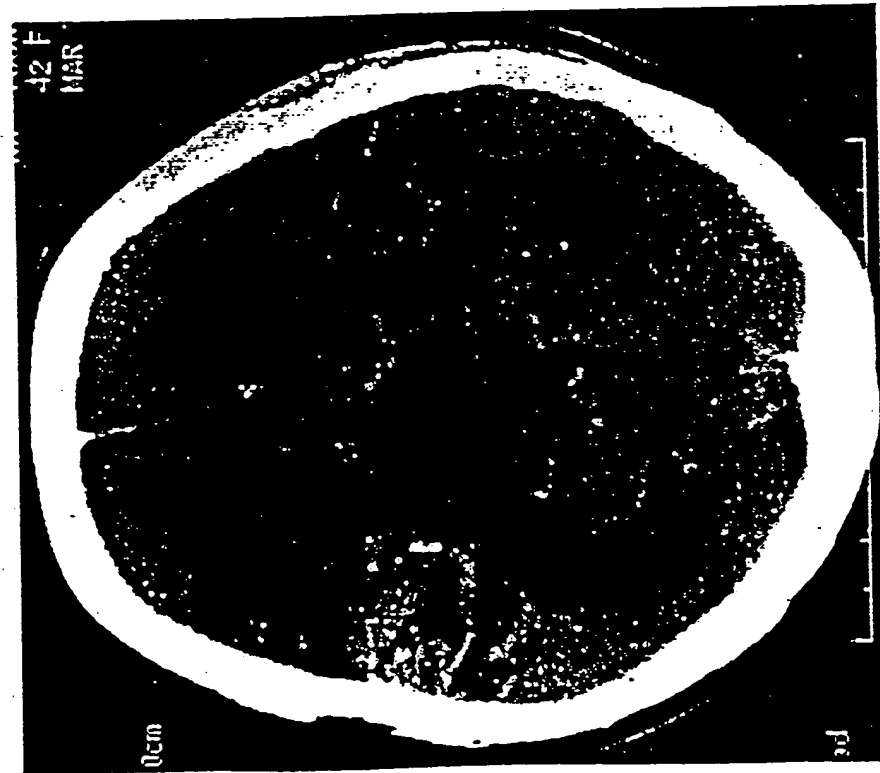
Planar image of breast tumor-bearing rats after administration of $^{99m}\text{Tc-EC}$ and $^{99m}\text{Tc-EC-Glucose(6)}$ ($100\mu\text{Ci/rat}$, iv.) showed that the tumor could be well visualized from 0.5-4 hours postinjection.

FIG. 81

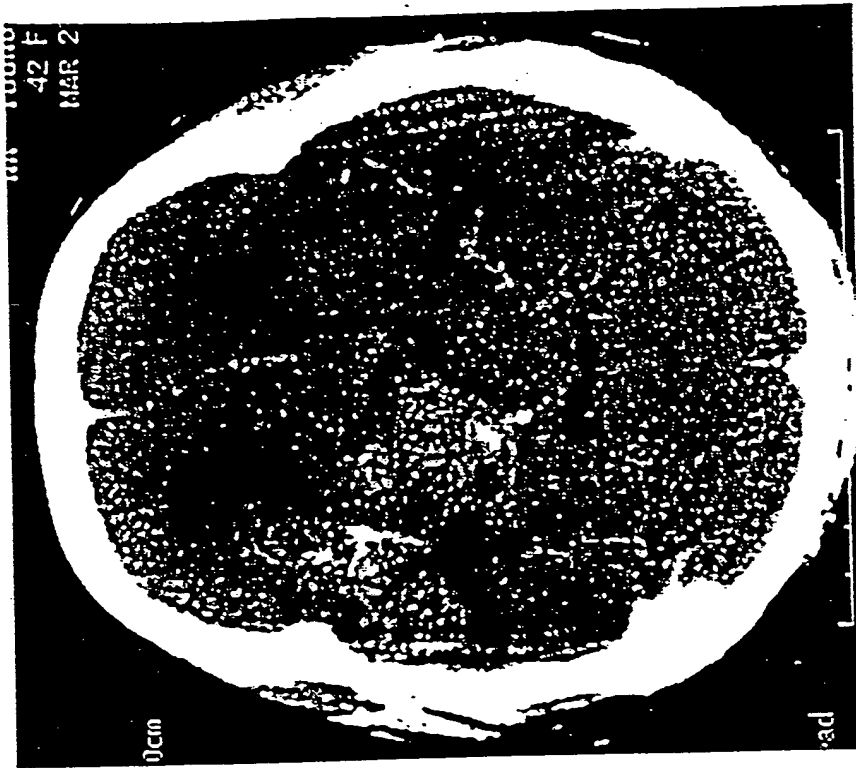
Planar image of breast tumor-bearing rats after administration of $^{99m}\text{Tc-EC}$ and $^{99m}\text{Tc-EC-deoxyglucose}$ ($100\mu\text{Ci/rat}$, iv.) showed that the tumor could be well visualized from 0.5-4 hours

Case 11/42

Dx : anaplastic astrocytoma



Pre OP



Post OP

NA YOUNG SOON

697800 F42

03770000 WONKWANG INTV HOSP



99mTc EC DG 1.5H

5



6



7



8



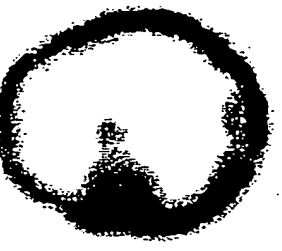
9



10



11



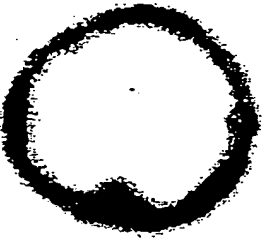
12



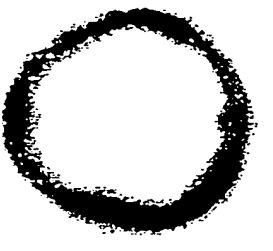
13



14



15



16



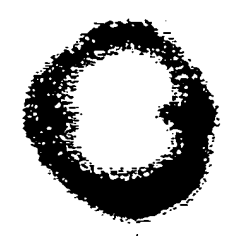
17



18



19



20

INFERIOR->SUPERIOR

EC--DG Scan

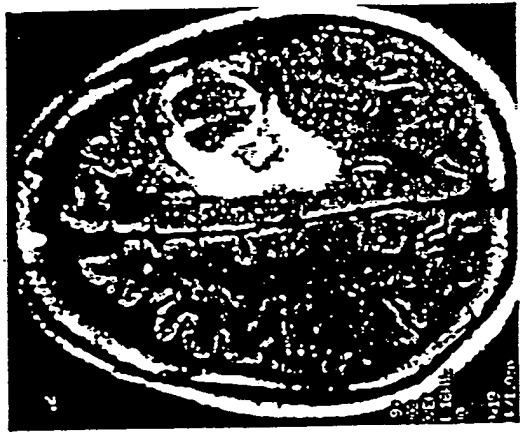
POD-25D

Case 1761

Di: anaplastic astrocytoma with hemorrhage



Pre -OP



Post-OP

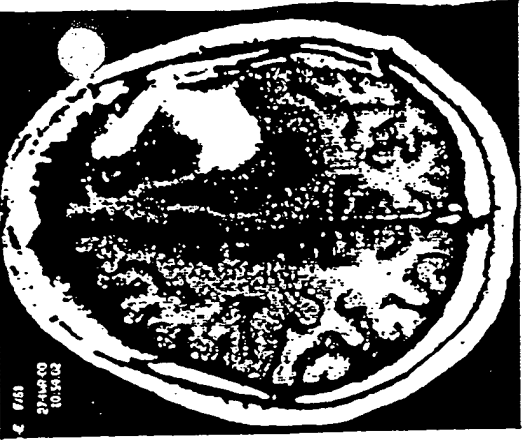
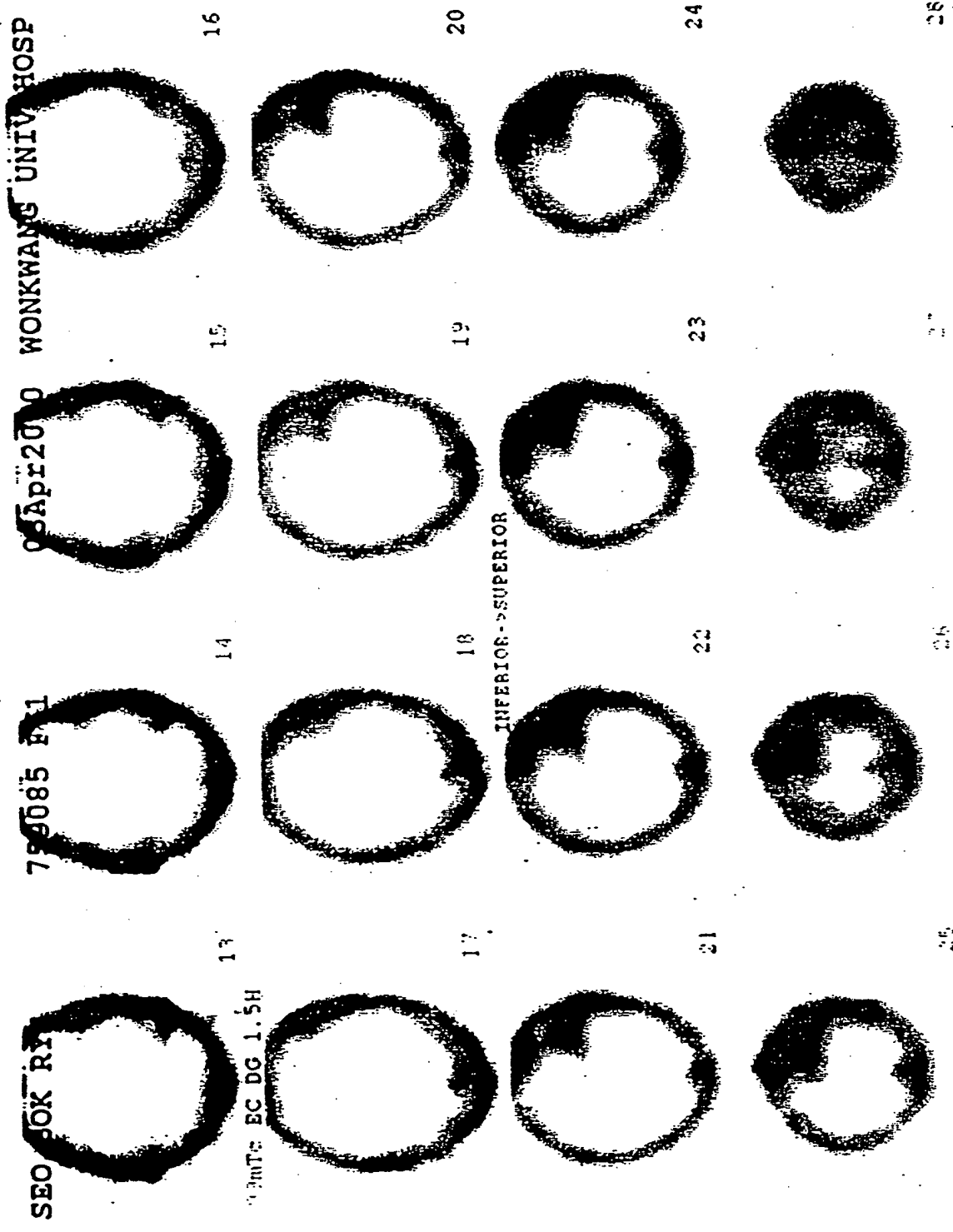


FIG. 83A MRI of a patient with hemorrhagic astrocytoma.



EC-DG Scan POD-26D

FIG. 83B SPECT with ^{99m}Tc -EC-DG of a patient with astrocytoma.

Case 5 : M/62

Dx : Meningioma



FIG. 84A

MRI of a patient with benign meningioma.

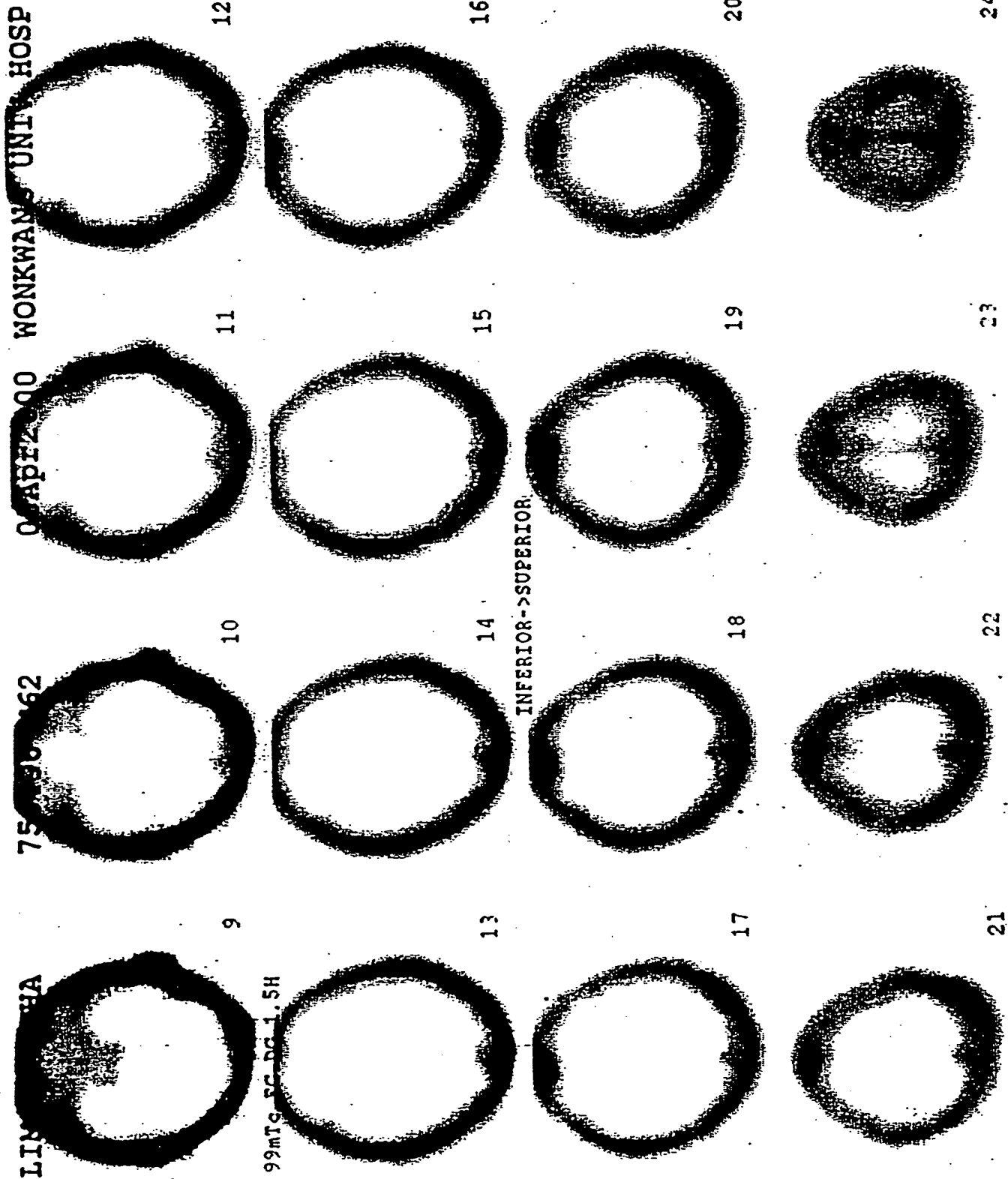


FIG. 84B SPECT with $^{99m}\text{Tc-EC-DG}$ of a patient with benign meningioma

CASE 4. M/77

Dx: Pul.module (only necrotic material on biopsy)

TB pleurisy

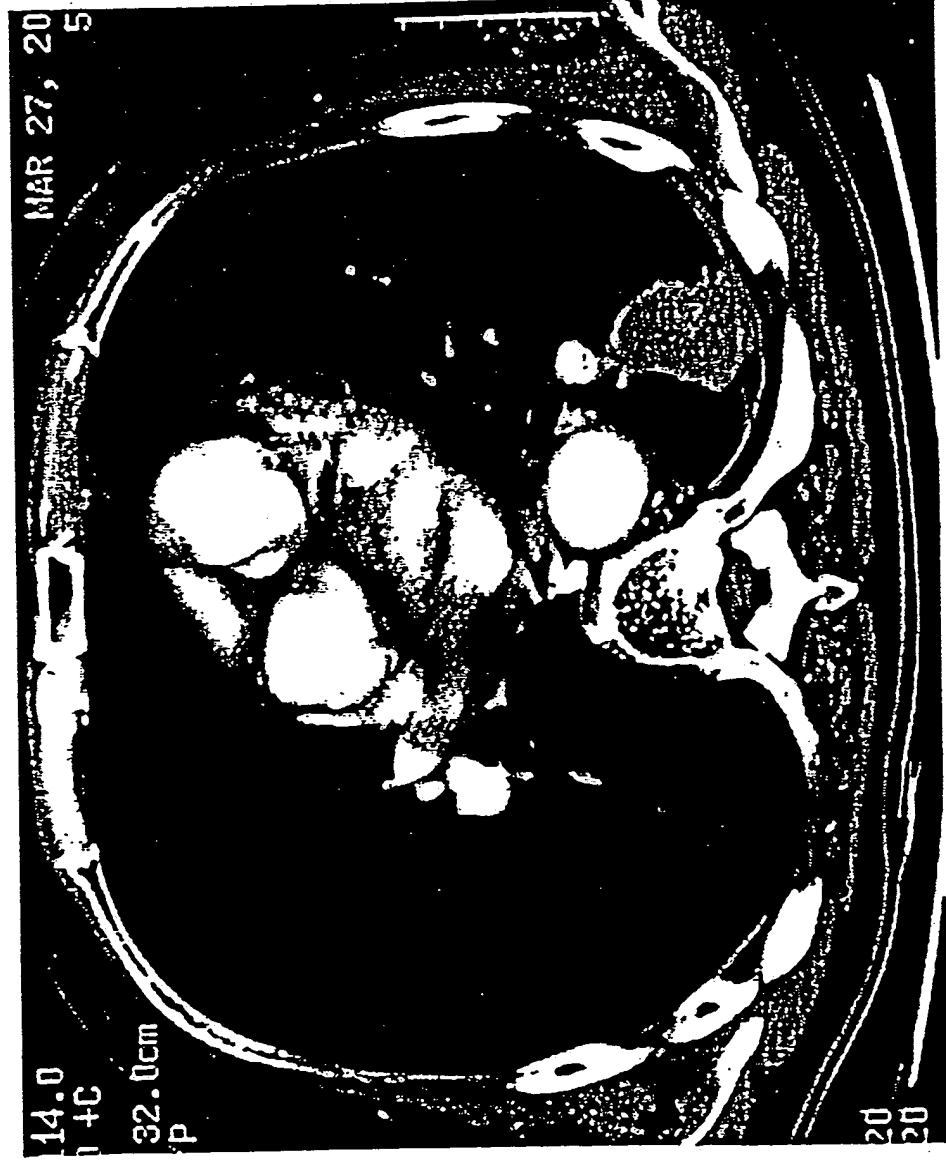


FIG. 85A CT of a patient with TB in lung.

WONKWANG HINFA-OSP

INFERIOR->SUPERIOR

SPECT with $^{99m}\text{Tc-EC-DG}$ of a patient with TB showed no focal

Case 5 : 59/M

Dx: Squamous carcinoma



Pre RTX



Post RTX

140.5
3
W 32.0cm
10/P

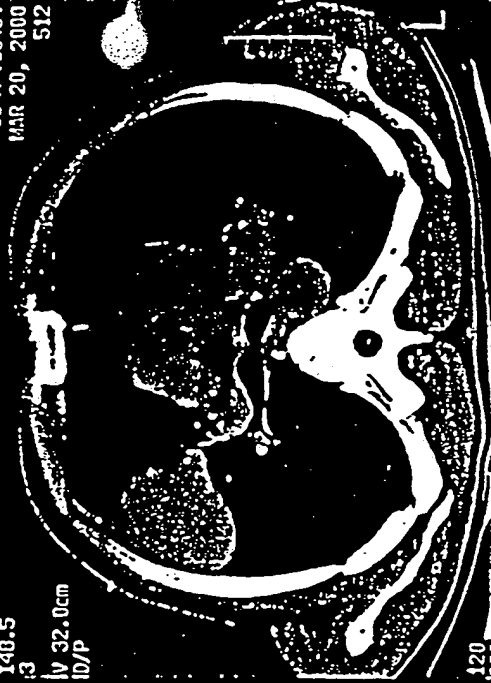
59 M 750434
MAR 20, 2000
512



Pre RTX

140.5
3
W 32.0cm
10/P

59 M 750434
MAR 20, 2000
512



Post RTX

JUNG KI WOON
EC DG 1H

758434 M59

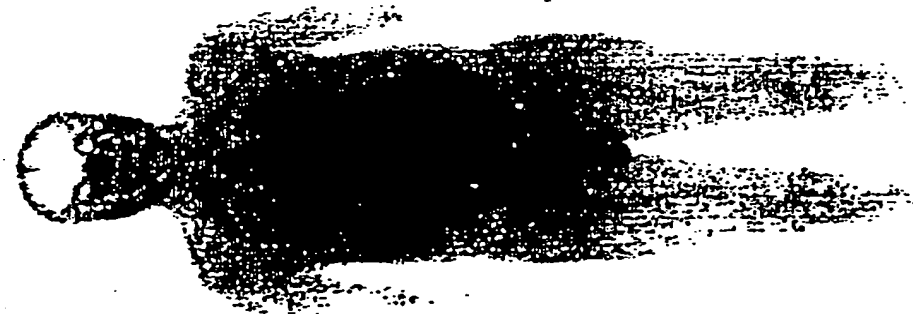
10Apr2000

WONKWANG UNIV HOSP



F

L



L



F



ANT

LUNG CANCER POST RTX 1HK

ANT

POST

EC

FIG. 86B

Whole body images of ^{99m}Tc -EC-DG of a patient with lung

cancer

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INFERIOR -> SUPERIOR



EC DG 1H 30 MIN LUNG CANCER POST RTX 1WK

FIG. 86C SPECT with ^{99m}Tc-EC-DG of a patient with lung cancer, the tumor showed focal intensified uptake.